```
=> fil reg
FILE 'REGISTRY' ENTERED AT 14:14:58 ON 09 MAR 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:    7 MAR 2003  HIGHEST RN 497212-14-3
DICTIONARY FILE UPDATES:   7 MAR 2003  HIGHEST RN 497212-14-3

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> d ide can l20

L20  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2003 ACS
RN   426832-86-2  REGISTRY
CN   Cyclopropaneacetic acid, 1-[[[(1R)-1-[3-[(1E)-2-(7-chloro-2-
     quinolinyl)ethenyl]phenyl]-3-[2-(1-hydroxy-1-methylethyl)phenyl]propyl]thi
     o]methyl]-, mixt. with 8-chloro-6,11-dihydro-11-(4-piperidinylidene)-5H-
     benzo[5,6]cyclohepta[1,2-b]pyridine (9CI)  (CA INDEX NAME)
FS   STEREOSEARCH
MF   C35 H36 Cl N O3 S . C19 H19 Cl N2
CI   MXS
SR   CA
LC   STN Files:   CA, CAPLUS, USPATFULL

     CM   1

     CRN  158966-92-8
     CMF  C35 H36 Cl N O3 S

Absolute stereochemistry.
Double bond geometry as shown.
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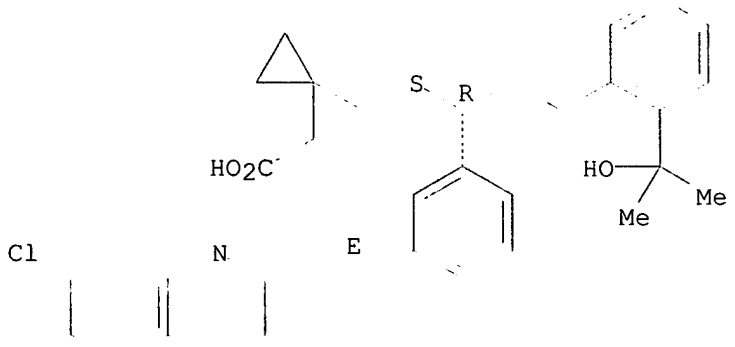

Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
C... 1507 – 703-308-4498
Ja... elaval@uspto.gov

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     CM   2
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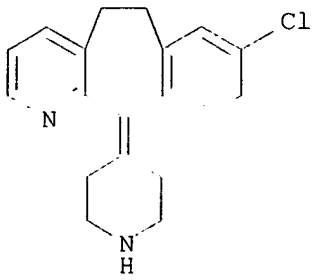
CRN 100643-71-8
CMF C19 H19 Cl N2

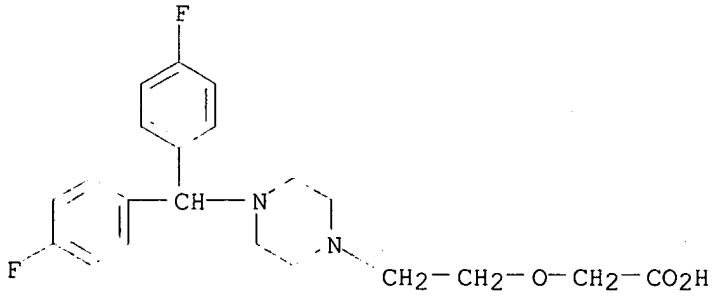


1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 136:380104

=> d ide can tot l11

L11 ANSWER 1 OF 8 REGISTRY COPYRIGHT 2003 ACS
RN 150756-35-7 REGISTRY
CN Acetic acid, [2-[4-[bis(4-fluorophenyl)methyl]-1-piperazinyl]ethoxy]-
(9CI) (CA INDEX NAME)
OTHER NAMES:
CN 2-[2-[4-[Bis(4-fluorophenyl)methyl]piperazin-1-yl]ethoxy]acetic acid
CN **Efletirizine**
CN [2-[4-[Bis(p-fluorophenyl)methyl]-1-piperazinyl]ethoxy]acetic acid
FS 3D CONCORD
MF C21 H24 F2 N2 O3
CI COM
SR World Health Organization
LC STN Files: ADISINSIGHT, ANABSTR, BIOBUSINESS, BIOSIS, CA, CAPLUS, DDFU, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, PHAR, PROMT, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
Other Sources: WHO



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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21 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:153552

REFERENCE 2: 138:73178

REFERENCE 3: 138:49929

REFERENCE 4: 137:247716

REFERENCE 5: 137:15819

REFERENCE 6: 136:380104

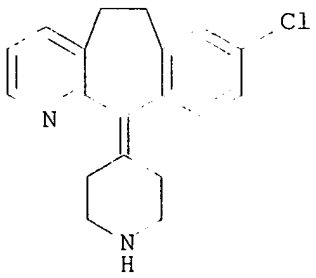
REFERENCE 7: 136:340592

REFERENCE 8: 135:111992

REFERENCE 9: 133:168392

REFERENCE 10: 132:284236

L11 ANSWER 2 OF 8 REGISTRY COPYRIGHT 2003 ACS
RN 100643-71-8 REGISTRY
CN 5H-Benzo[5,6]cyclohepta[1,2-b]pyridine, 8-chloro-6,11-dihydro-11-(4-piperidinylidene)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 8-Chloro-11-(4-piperidylidene)-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridine
CN Aerius
CN Clarinex
CN **Descarboethoxyloratadine**
CN **Desloratadine**
CN Neoclarytin
CN Sch 34117
MF C19 H19 Cl N2
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, MRCK*, PHAR, PROMT, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

156 REFERENCES IN FILE CA (1962 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
159 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:158851

REFERENCE 2: 138:126978

REFERENCE 3: 138:100180

REFERENCE 4: 138:78570

REFERENCE 5: 138:78456

REFERENCE 6: 138:73178

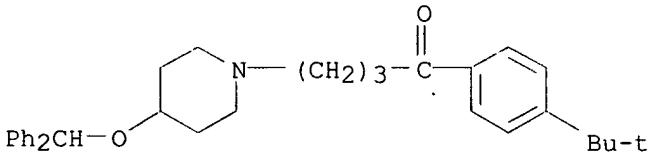
REFERENCE 7: 138:49929

REFERENCE 8: 138:49404

REFERENCE 9: 138:32765

REFERENCE 10: 138:316

L11 ANSWER 3 OF 8 REGISTRY COPYRIGHT 2003 ACS
RN 90729-43-4 REGISTRY
CN 1-Butanone, 1-[4-(1,1-dimethylethyl)phenyl]-4-[4-(diphenylmethoxy)-1-piperidinyl]- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Ebastin
CN **Ebastine**
FS 3D CONCORD
MF C32 H39 N O2
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CBNB, CHEMCATS, CIN, CSCHEM, DDFU, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, MRCK*, PHAR, PROMT, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

157 REFERENCES IN FILE CA (1962 TO DATE)
8 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
158 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:147617

REFERENCE 2: 138:130864

REFERENCE 3: 138:73178

REFERENCE 4: 138:66570

REFERENCE 5: 138:49929

REFERENCE 6: 138:250

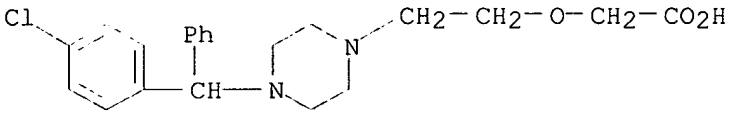
REFERENCE 7: 137:346182

REFERENCE 8: 137:304292

REFERENCE 9: 137:299872

REFERENCE 10: 137:289046

L11 ANSWER 4 OF 8 REGISTRY COPYRIGHT 2003 ACS
RN 83881-51-0 REGISTRY
CN Acetic acid, [2-[4-[(4-chlorophenyl)phenylmethyl]-1-piperazinyl]ethoxy]-
(9CI) (CA INDEX NAME)
OTHER NAMES:
CN **Cetirizine**
FS 3D CONCORD
DR 130018-86-9
MF C21 H25 Cl N2 O3
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, MRCK*, NIOSHTIC, PHAR, PROMT, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: WHO



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

446 REFERENCES IN FILE CA (1962 TO DATE)
9 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
446 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:130864

REFERENCE 2: 138:73178

REFERENCE 3: 138:61370

REFERENCE 4: 138:49929

REFERENCE 5: 138:11117

REFERENCE 6: 138:225

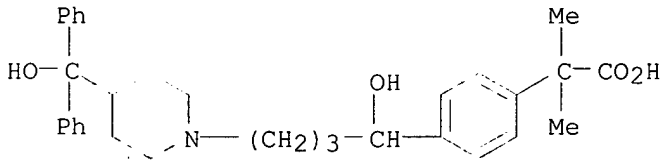
REFERENCE 7: 137:389216

REFERENCE 8: 137:362836

REFERENCE 9: 137:362115

REFERENCE 10: 137:345929

L11 ANSWER 5 OF 8 REGISTRY COPYRIGHT 2003 ACS
RN 83799-24-0 REGISTRY
CN Benzeneacetic acid, 4-[1-hydroxy-4-[4-(hydroxydiphenylmethyl)-1-piperidinyl]butyl]-.alpha.,.alpha.-dimethyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 4-[4-[4-(Hydroxydiphenylmethyl)-1-piperidinyl]-1-hydroxybutyl]-.alpha.,.alpha.-dimethylphenylacetic acid
CN Carboxyterfenadine
CN **Fexofenadine**
CN MDL 16455
CN Terfenadine acid metabolite
CN Terfenadine carboxylate
FS 3D CONCORD
DR 159389-12-5, 76815-58-2
MF C32 H39 N O4
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BIOBUSINESS, BIOSIS, CA, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, MRCK*, PROMT, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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217 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:158763

REFERENCE 2: 138:147480

REFERENCE 3: 138:147184

REFERENCE 4: 138:133411

REFERENCE 5: 138:130864

REFERENCE 6: 138:126952

REFERENCE 7: 138:122559

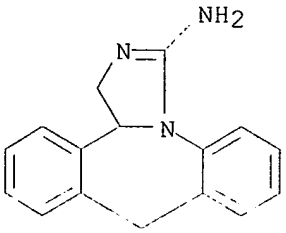
REFERENCE 8: 138:100652

REFERENCE 9: 138:73178

REFERENCE 10: 138:73082

L11 ANSWER 6 OF 8 REGISTRY COPYRIGHT 2003 ACS
RN 80012-43-7 REGISTRY
CN 1H-Dibenz[c,f]imidazo[1,5-a]azepin-3-amine, 9,13b-dihydro- (9CI) (CA INDEX NAME)
OTHER NAMES:

CN (.+-.)-Epinastine
CN **Epinastine**
CN WAL 801
FS 3D CONCORD
DR 134507-59-8
MF C16 H15 N3
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CIN, DDFU, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, MRCK*, PHAR, PROMT, SYNTHLINE, TOXCENTER, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

125 REFERENCES IN FILE CA (1962 TO DATE)
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125 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:73178

REFERENCE 2: 138:49929

REFERENCE 3: 137:362836

REFERENCE 4: 137:358089

REFERENCE 5: 137:268446

REFERENCE 6: 137:247716

REFERENCE 7: 137:72847

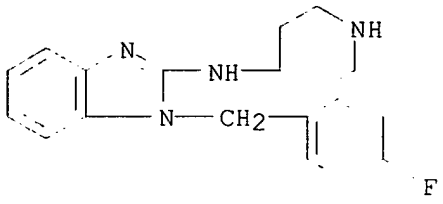
REFERENCE 8: 137:41740

REFERENCE 9: 136:380104

REFERENCE 10: 136:374833

L11 ANSWER 7 OF 8 REGISTRY COPYRIGHT 2003 ACS
RN 75970-99-9 REGISTRY
CN 1H-Benzimidazol-2-amine, 1-[(4-fluorophenyl)methyl]-N-4-piperidinyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 1-(4-Fluorobenzyl)-2-(4-piperidylamino)benzimidazole
CN 1-(4-Fluorophenylmethyl)-2-(4-piperidylamino)benzimidazole
CN **Norastemizole**
CN Soltara
CN T 1348
CN Tecastemizole

MF C19 H21 F N4
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CEN, CIN, CSCHEM, DDFU, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, PHAR, PROMT, SYNTHLINE, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

62 REFERENCES IN FILE CA (1962 TO DATE)
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REFERENCE 1: 138:127034

REFERENCE 2: 138:73178

REFERENCE 3: 138:49929

REFERENCE 4: 137:375287

REFERENCE 5: 137:247716

REFERENCE 6: 137:241682

REFERENCE 7: 137:109489

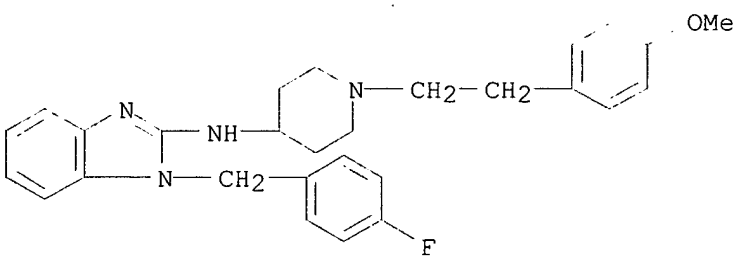
REFERENCE 8: 136:380104

REFERENCE 9: 136:355482

REFERENCE 10: 136:340592

L11 ANSWER 8 OF 8 REGISTRY COPYRIGHT 2003 ACS
RN 68844-77-9 REGISTRY
CN 1H-Benzimidazol-2-amine, 1-[(4-fluorophenyl)methyl]-N-[1-[2-(4-methoxyphenyl)ethyl]-4-piperidinyl]- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Astemisan
CN **Astemizole**
CN Hismanal
CN Histamen
CN Histaminos
CN Histazol
CN Kelp
CN Laridal
CN Metodik
CN Novo-Nastizol A
CN Paralergin
CN R 42512
CN R 43512
CN Retolen

CN Waruzol
MF C28 H31 F N4 O
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, HSDB*, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PHAR, PROMT, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

418 REFERENCES IN FILE CA (1962 TO DATE)
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420 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:147617

REFERENCE 2: 138:131056

REFERENCE 3: 138:78456

REFERENCE 4: 138:73178

REFERENCE 5: 138:66653

REFERENCE 6: 138:49929

REFERENCE 7: 138:44736

REFERENCE 8: 138:33365

REFERENCE 9: 138:32765

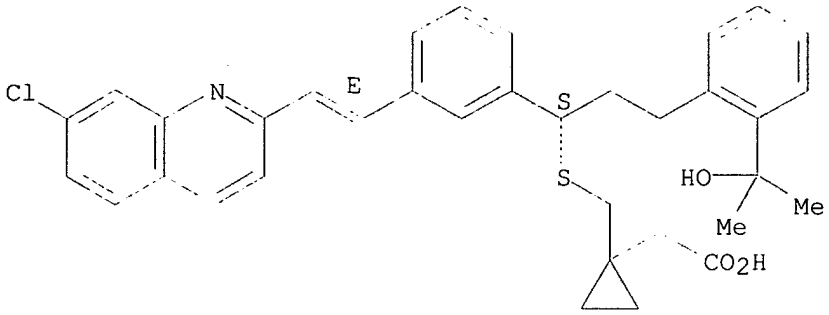
REFERENCE 10: 137:358177

=> d ide can tot l18

L18 ANSWER 1 OF 4 REGISTRY COPYRIGHT 2003 ACS
RN 220927-27-5 REGISTRY
CN Cyclopropaneacetic acid, 1-[[[(1S)-1-[3-[(1E)-2-(7-chloro-2-quinolinyl)ethenyl]phenyl]-3-[2-(1-hydroxy-1-methylethyl)phenyl]propyl]thio]methyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C35 H36 Cl N O3 S**
CI COM

SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.
Double bond geometry as shown.



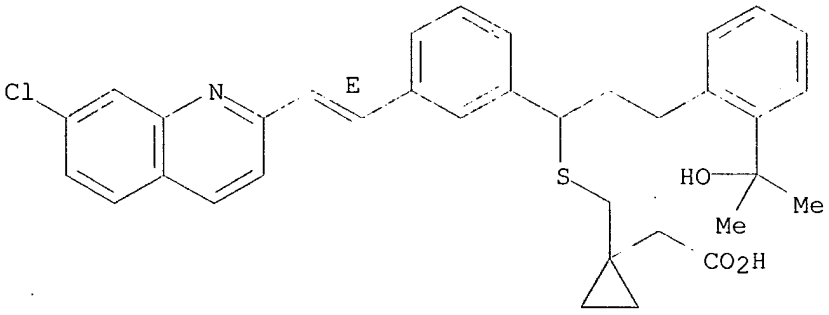
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 130:213725

L18 ANSWER 2 OF 4 REGISTRY COPYRIGHT 2003 ACS
RN 220927-26-4 REGISTRY
CN Cyclopropaneacetic acid, 1-[[[1-[3-[(1E)-2-(7-chloro-2-quinolinyl)ethenyl]phenyl]-3-[2-(1-hydroxy-1-methylethyl)phenyl]propyl]thio]methyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C35 H36 Cl N O3 S**
SR CA
LC STN Files: CA, CAPLUS

Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

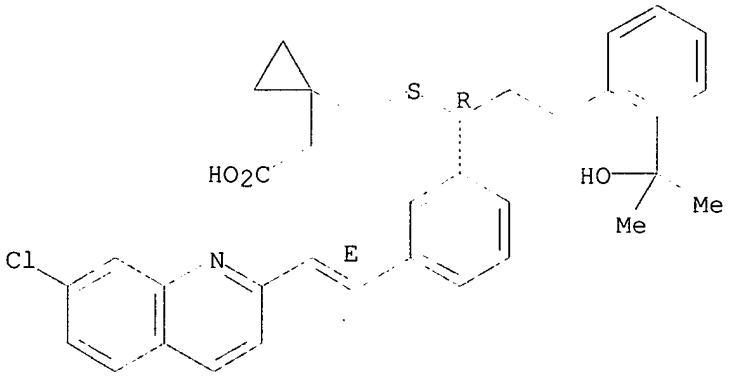
1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 130:213725

L18 ANSWER 3 OF 4 REGISTRY COPYRIGHT 2003 ACS
RN 158966-92-8 REGISTRY
CN Cyclopropaneacetic acid, 1-[[[(1R)-1-[3-[(1E)-2-(7-chloro-2-

quinolinyl)ethenyl]phenyl]-3-[2-(1-hydroxy-1-methylethyl)phenyl]propyl]thi
o]methyl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Cyclopropaneacetic acid, 1-[[[1-[3-[2-(7-chloro-2-
quinolinyl)ethenyl]phenyl]-3-[2-(1-hydroxy-1-methylethyl)phenyl]propyl]thi
o]methyl]-, [R-(E)]-
OTHER NAMES:
CN **Montelukast**
FS STEREOSEARCH
MF **C35 H36 Cl N O3 S**
CI COM
SR World Health Organization
LC STN Files: ADISINSIGHT, ADISNEWS, BIOBUSINESS, BIOSIS, BIOTECHNO, CA,
CANCERLIT, CAPLUS, CHEMCATS, CIN, DDFU, DIOGENES, DRUGNL, DRUGPAT,
DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, MRCK*, PHARMASEARCH, PROMT,
SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

153 REFERENCES IN FILE CA (1962 TO DATE)
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153 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:130852

REFERENCE 2: 138:117473

REFERENCE 3: 138:117398

REFERENCE 4: 138:117386

REFERENCE 5: 138:73178

REFERENCE 6: 138:39187

REFERENCE 7: 138:19255

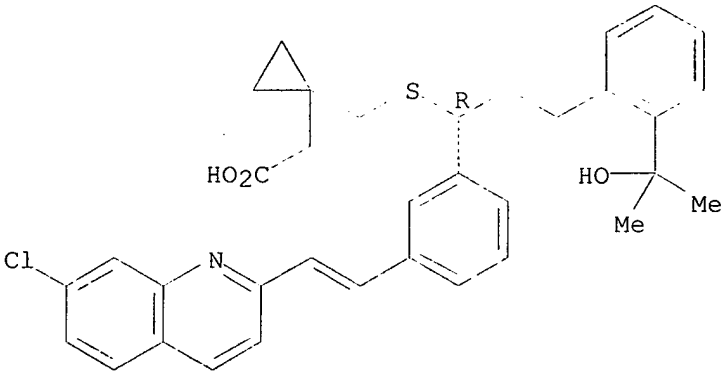
REFERENCE 8: 137:379839

REFERENCE 9: 137:362833

REFERENCE 10: 137:362325

L18 ANSWER 4 OF 4 REGISTRY COPYRIGHT 2003 ACS
RN 142522-28-9 REGISTRY
CN Cyclopropaneacetic acid, 1-[[[1-[3-[2-(7-chloro-2-quinolinyl)ethenyl]phenyl]-3-[2-(1-hydroxy-1-methylethyl)phenyl]propyl]thio]methyl]-, (R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C35 H36 Cl N O3 S**
CI COM
SR CA
LC STN Files: ADISINSIGHT, CA, CAPLUS, DRUGPAT, DRUGUPDATES, SYNTHLINE, USPATFULL

Absolute stereochemistry.
Double bond geometry unknown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1962 TO DATE)
3 REFERENCES IN FILE CAPLUS (1962 TO DATE)

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REFERENCE 2: 123:313787

REFERENCE 3: 117:90163

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 14:16:14 ON 09 MAR 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 9 Mar 2003 VOL 138 ISS 11
FILE LAST UPDATED: 7 Mar 2003 (20030307/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all hitstr tot l89

L89 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2003 ACS
AN **2002:392238** HCAPLUS
DN **136:380104**
TI **Antihistamine**, alone or with **leukotriene** antagonist, for the prevention and treatment of cardiovascular disease
IN **Harris, Alan G.; Medeiros, Paul T.**
PA **Schering Corporation, USA**
SO U.S. Pat. Appl. Publ., 8 pp.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61K031-496
ICS A61K031-473
NCL 514290000
CC 1-8 (Pharmacology)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2002061902	A1	20020523	US 2001-21189	20011030 <--
WO 2002067938	A2	20020906	WO 2001-US45481	20011026 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2000-244365P P 20001030 <--
AB Methods are disclosed for treating and/or preventing a cardiovascular disease in a human suffering from an allergic and/or inflammatory condition of the skin or upper airway passages or cardiovascular disease by administering an effective amt. of an **antihistamine**, preferably **desloratadine**, alone or in **admixt.** with an effective amt. of at least one **leukotriene** antagonist, preferably **montelukast**.
ST **antihistamine leukotriene** antagonist cardiovascular disease; **desloratadine montelukast** cardiovascular disease
IT Animal cell line
(HUVEC; **antihistamine**, alone or with **leukotriene** antagonist, for prevention and treatment of cardiovascular disease)
IT **Nose**
(allergic rhinitis, seasonal and perennial; **antihistamine**, alone or with **leukotriene** antagonist, for prevention and treatment of cardiovascular disease)
IT Asthma
Dermatitis
(allergic; **antihistamine**, alone or with **leukotriene** antagonist, for prevention and treatment of cardiovascular disease)
IT **Respiratory tract**
(allergy, **upper** airway; **antihistamine**, alone or with **leukotriene** antagonist, for prevention and treatment of

cardiovascular disease)

IT **Antihistamines**
Cardiovascular agents
Dermatitis
Human
Leukotriene antagonists
Urticaria
(**antihistamine**, alone or with **leukotriene** antagonist, for prevention and treatment of cardiovascular disease)

IT **Dermatitis**
(atopic; **antihistamine**, alone or with **leukotriene** antagonist, for prevention and treatment of cardiovascular disease)

IT Eosinophil
(chemotaxis and adhesion; **antihistamine**, alone or with **leukotriene** antagonist, for prevention and treatment of cardiovascular disease)

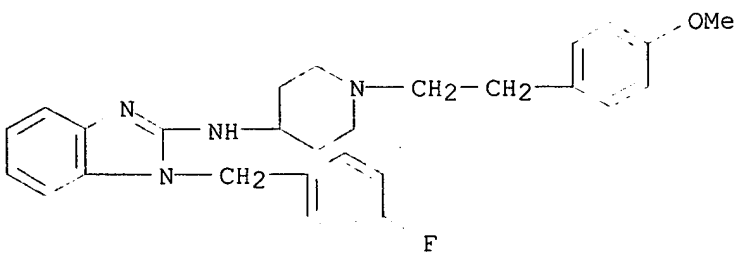
IT Adhesion, biological
Chemotaxis
(eosinophil; **antihistamine**, alone or with **leukotriene** antagonist, for prevention and treatment of cardiovascular disease)

IT **Respiratory tract**
(inflammation, **upper** airway; **antihistamine**, alone or with **leukotriene** antagonist, for prevention and treatment of cardiovascular disease)

IT **68844-77-9, Astemizole 75970-99-9, Norastemizole 80012-43-7, Epinastine 83799-24-0, Fexofenadine 83881-51-0, Cetirizine 90729-43-4, Ebastine 100643-71-8, Desloratadine 150756-35-7, Efletirizine 158966-92-8, Montelukast 426832-86-2**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**antihistamine**, alone or with **leukotriene** antagonist, for prevention and treatment of cardiovascular disease)

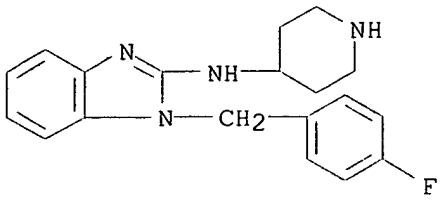
IT **68844-77-9, Astemizole 75970-99-9, Norastemizole 80012-43-7, Epinastine 83799-24-0, Fexofenadine 83881-51-0, Cetirizine 90729-43-4, Ebastine 100643-71-8, Desloratadine 150756-35-7, Efletirizine 158966-92-8, Montelukast 426832-86-2**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**antihistamine**, alone or with **leukotriene** antagonist, for prevention and treatment of cardiovascular disease)

RN 68844-77-9 HCAPLUS
CN 1H-Benzimidazol-2-amine, 1-[(4-fluorophenyl)methyl]-N-[1-[2-(4-methoxyphenyl)ethyl]-4-piperidinyl]- (9CI) (CA INDEX NAME)

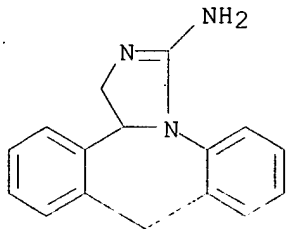


RN 75970-99-9 HCAPLUS

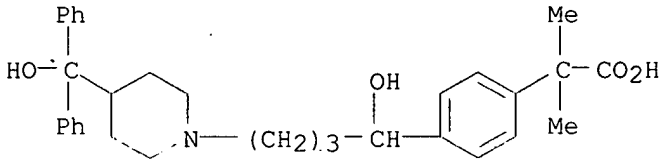
CN 1H-Benzimidazol-2-amine, 1-[(4-fluorophenyl)methyl]-N-4-piperidinyl- (9CI) (CA INDEX NAME)



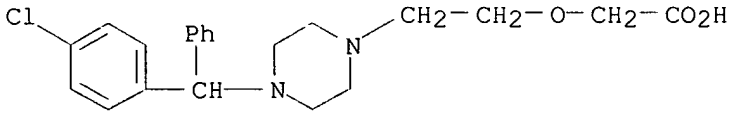
RN 80012-43-7 HCAPLUS
CN 1H-Dibenz[c,f]imidazo[1,5-a]azepin-3-amine, 9,13b-dihydro- (9CI) (CA INDEX NAME)



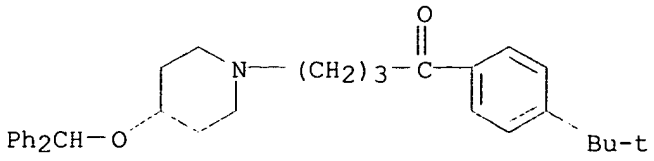
RN 83799-24-0 HCAPLUS
CN Benzeneacetic acid, 4-[1-hydroxy-4-[4-(hydroxydiphenylmethyl)-1-piperidinyl]butyl]-.alpha.,.alpha.-dimethyl- (9CI) (CA INDEX NAME)



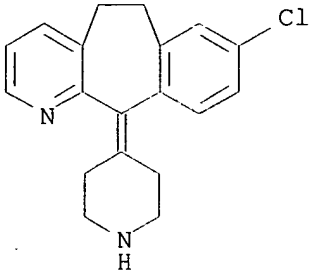
RN 83881-51-0 HCAPLUS
CN Acetic acid, [2-[4-[(4-chlorophenyl)phenylmethyl]-1-piperazinyl]ethoxy]- (9CI) (CA INDEX NAME)



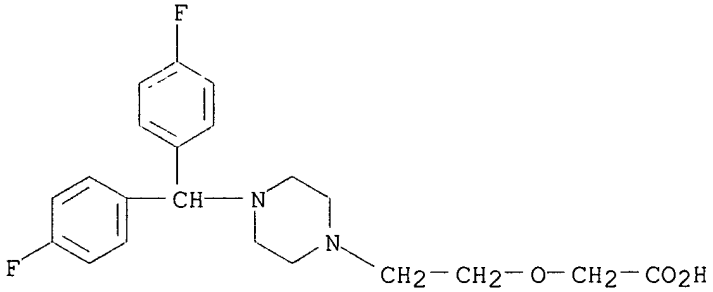
RN 90729-43-4 HCAPLUS
CN 1-Butanone, 1-[4-(1,1-dimethylethyl)phenyl]-4-[4-(diphenylmethoxy)-1-piperidinyl]- (9CI) (CA INDEX NAME)



RN 100643-71-8 HCAPLUS
CN 5H-Benzo[5,6]cyclohepta[1,2-b]pyridine, 8-chloro-6,11-dihydro-11-(4-piperidinylidene)- (9CI) (CA INDEX NAME)

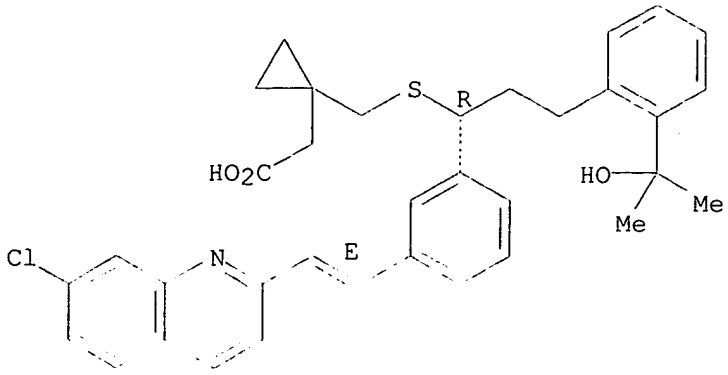


RN 150756-35-7 HCAPLUS
CN Acetic acid, [2-[4-[bis(4-fluorophenyl)methyl]-1-piperazinyl]ethoxy]- (9CI) (CA INDEX NAME)



RN 158966-92-8 HCAPLUS
CN Cyclopropaneacetic acid, 1-[[[(1R)-1-[3-[(1E)-2-(7-chloro-2-quinolinyl)ethenyl]phenyl]-3-[2-(1-hydroxy-1-methylethyl)phenyl]propyl]thio]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

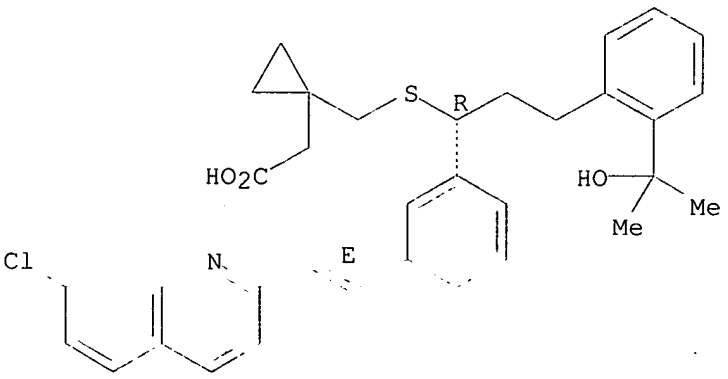


RN 426832-86-2 HCAPLUS
CN Cyclopropaneacetic acid, 1-[[[(1R)-1-[3-[(1E)-2-(7-chloro-2-quinolinyl)ethenyl]phenyl]-3-[2-(1-hydroxy-1-methylethyl)phenyl]propyl]thio]methyl]-, mixt. with 8-chloro-6,11-dihydro-11-(4-piperidinylidene)-5H-benzo[5,6]cyclohepta[1,2-b]pyridine (9CI) (CA INDEX NAME)

CM 1

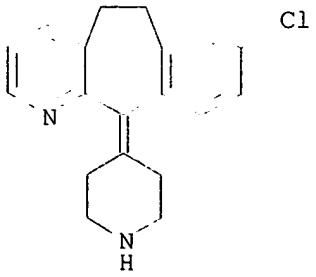
CRN 158966-92-8
CMF C35 H36 Cl N O3 S

Absolute stereochemistry.
Double bond geometry as shown.



CM 2

CRN 100643-71-8
CMF C19 H19 Cl N2



L89 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2003 ACS
AN **2001:780657** HCAPLUS
DN **135:335151**
TI Method and **compositions** for the treatment of allergic conditions using PGD2 receptor antagonists
IN Jones, Thomas R.
PA Merck Frosst Canada + Co., Can.
SO PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-00
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 25
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001078697	A2	20011025	WO 2001-CA491	20010409 <--
WO 2001078697	A3	20020801		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2001051624	A1	20011213	US 2001-818885	20010327 <--
EP 1274457	A2	20030115	EP 2001-923433	20010409 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRAI US 2000-196641P	P	20000412 <--		
WO 2001-CA491	W	20010409		

AB A method for the treatment of allergic conditions, e.g., allergic rhinitis, **comprises** administering an effective amt. of a prostaglandin D2 (PGD2) receptor antagonist and an effective amt. of at least one other therapeutically active compd. selected from a **histamine** H1 antagonist and a **leukotriene** antagonist. The **histamine** H1 antagonist is selected from **loratadine**, **descarboethoxyloratadine**, **cetirizine**, levocetirizine and **fexofenadine**, while the **leukotriene** D4 antagonist is selected from zafirlukast, **montelukast** and pranlukast. The allergic condition is allergic rhinitis. For example, the synthesis of 2-[(1R)-9-(4-chlorobenzyl)-8-((R)-methylsulfinyl)-2,3,4,9-tetrahydro-1H-carbazol-1-yl]acetic acid and 2-[(1R)-9-(4-chlorobenzyl)-8-((S)-methylsulfinyl)-2,3,4,9-tetrahydro-1H-carbazol-1-yl]acetic acid (I) was described. The single administration of the **histamine** H1 antagonist mepyramine (5 mg/kg, i.p.) or compd. I (1 mg/kg, i.p.) 60 min prior to ovalbumin nasal antigen challenge in guinea pigs had no significant effect on the increase in intranasal pressure. However, in similar exptl. conditions, the increase in intranasal pressure produced by ovalbumin was significantly blocked by the **combination** of mepyramine (5 mg/kg, i.p.) and compd. I (0.3 or 1 mg mg/kg, i.p.).

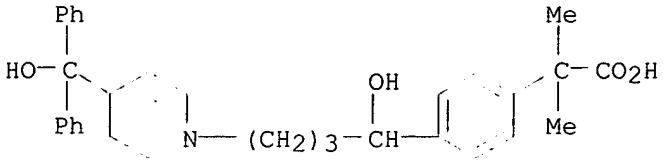
ST prostaglandin receptor **leukotriene** antagonist **antihistamine** antiallergy; nasal spray allergic rhinitis

IT Prostanoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(DP, antagonists; **compns**. contg. prostaglandin D2 receptor antagonist, **antihistamine** and **leukotriene** antagonist for allergy treatment)

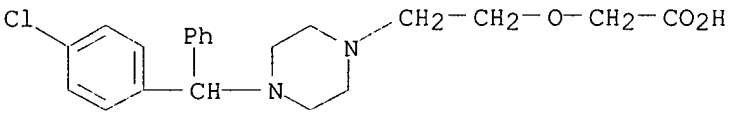
IT **Antihistamines**
(**H1**; **compns**. contg. prostaglandin D2 receptor antagonist, **antihistamine** and **leukotriene** antagonist for allergy treatment)
IT **Nose**
(allergic rhinitis; **compns**. contg. prostaglandin D2 receptor antagonist, **antihistamine** and **leukotriene** antagonist for allergy treatment)
IT Allergy inhibitors
Leukotriene antagonists
(**compns**. contg. prostaglandin D2 receptor antagonist, **antihistamine** and **leukotriene** antagonist for allergy treatment)
IT Drug delivery systems
(nasal sprays; **compns**. contg. prostaglandin D2 receptor antagonist, **antihistamine** and **leukotriene** antagonist for allergy treatment)
IT 73836-78-9, **Leukotriene** D4
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; **compns**. contg. prostaglandin D2 receptor antagonist, **antihistamine** and **leukotriene** antagonist for allergy treatment)
IT 367958-38-1P 367958-41-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**compns**. contg. prostaglandin D2 receptor antagonist, **antihistamine** and **leukotriene** antagonist for allergy treatment)
IT 59-33-6, Mepyramine 79794-75-5, **Loratadine 83799-24-0**
, **Fexofenadine 83881-51-0, Cetirizine**
100643-71-8, Descarboethoxyloratadine 103177-37-3,
Pranlukast 107753-78-6, Zafirlukast 130018-77-8, Levocetirizine
158966-92-8, Montelukast
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**compns**. contg. prostaglandin D2 receptor antagonist, **antihistamine** and **leukotriene** antagonist for allergy treatment)
IT 870-50-8, Di-tert-butyl azodicarboxylate 2987-53-3, 2-(Methylthio)aniline 19614-16-5 24731-17-7, Ethyl 2-cyclohexanoneacetate
RL: RCT (Reactant); RACT (Reactant or reagent)
(**compns**. contg. prostaglandin D2 receptor antagonist, **antihistamine** and **leukotriene** antagonist for allergy treatment)
IT 60481-33-6P 88965-67-7P 121083-42-9P 367958-15-4P 367958-20-1P
367958-28-9P 367958-31-4P 367958-35-8P 367958-36-9P 369644-71-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(**compns**. contg. prostaglandin D2 receptor antagonist, **antihistamine** and **leukotriene** antagonist for allergy treatment)
IT 41598-07-6, Prostaglandin D2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(receptors, antagonists; **compns**. contg. prostaglandin D2 receptor antagonist, **antihistamine** and **leukotriene** antagonist for allergy treatment)
IT **83799-24-0, Fexofenadine 83881-51-0,**
Cetirizine 100643-71-8, Descarboethoxyloratadine
158966-92-8, Montelukast
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**compns**. contg. prostaglandin D2 receptor antagonist, **antihistamine** and **leukotriene** antagonist for allergy treatment)

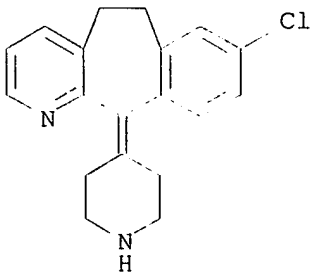
RN 83799-24-0 HCAPLUS
CN Benzeneacetic acid, 4-[1-hydroxy-4-[4-(hydroxydiphenylmethyl)-1-piperidinyl]butyl]-.alpha.,.alpha.-dimethyl- (9CI) (CA INDEX NAME)



RN 83881-51-0 HCAPLUS
CN Acetic acid, [2-[4-[(4-chlorophenyl)phenylmethyl]-1-piperazinyl]ethoxy]- (9CI) (CA INDEX NAME)

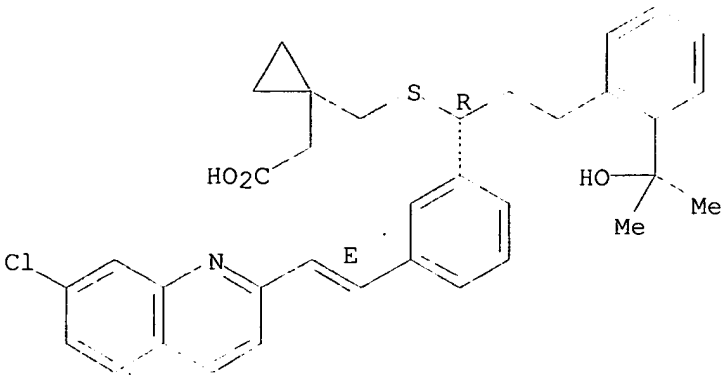


RN 100643-71-8 HCAPLUS
CN 5H-Benzo[5,6]cyclohepta[1,2-b]pyridine, 8-chloro-6,11-dihydro-11-(4-piperidinylidene)- (9CI) (CA INDEX NAME)



RN 158966-92-8 HCAPLUS
CN Cyclopropaneacetic acid, 1-[[[(1R)-1-[3-[(1E)-2-(7-chloro-2-quinolinyl)ethenyl]phenyl]-3-[2-(1-hydroxy-1-methylethyl)phenyl]propyl]thio]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L89 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2003 ACS
AN **2001:617861** HCAPLUS
DN **135:185482**
TI Novel **combination** of non-sedative anti-**histamines** containing substances which influence the action of **leukotriene**, for treating rhinitis/conjunctivitis
IN Poppe, Hildegard; Engel, Juergen; Szelenyi, Istvan
PA Asta Medica Aktiengesellschaft, Germany
SO PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DT Patent
LA German
IC ICM A61K045-00
CC 63-6 (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001060407	A2	20010823	WO 2001-EP1190	20010205 <--
	WO 2001060407	A3	20020307		
	W: AU, BG, BR, BY, CN, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
	DE 10007203	A1	20010823	DE 2000-10007203	20000217 <--
	EP 1265615	A2	20021218	EP 2001-911591	20010205 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2001025040	A1	20010927	US 2001-784640	20010215 <--
	US 6436924	B2	20020820		
	NO 2002003818	A	20020812	NO 2002-3818	20020812 <--
PRAI	DE 2000-10007203	A	20000217 <--		
	WO 2001-EP1190	W	20010205		

AB The invention relates to a pharmaceutical **combination** to be administered topically or orally of a non-sedative anti-**histamine**, with the exception of compds. of the **loratadine** type, and a **leukotriene** antagonist, selected from a **leukotriene** D4 antagonist, or a 5-lipoxygenase inhibitor, or a FLAP antagonist and optionally conventional, physiol. harmless supports, extenders and auxiliary agents, for the prophylaxis and treatment of allergic and/or vasomotor rhinitis or allergic conjunctivitis. Thus a nasal spray contained in 100 mL aq. soln. (g): **montelukast** 1.0000 azelastine hydrochloride 0.1000; Avicel RC591 1.1000; Polysorbat 80 0.1000; sorbitol soln. (70%) 6.0000; sodium EDTA 0.0500; benzalkonium chloride 0.0200.
ST **antihistamine leukotriene** antagonist **combination** eye nose drop rhinitis conjunctivitis

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(FLAP (arachidonate lipoxygenase-activating protein), antagonist; **combination** of non-sedative anti-**histamines** contg. substances which influence action of **leukotriene**, for treating rhinitis/conjunctivitis)

IT Eye, disease
(allergic conjunctivitis; **combination** of non-sedative anti-**histamines** contg. substances which influence action of **leukotriene**, for treating rhinitis/conjunctivitis)

IT **Antihistamines**
Leukotriene antagonists
(**combination** of non-sedative anti-**histamines** contg. substances which influence action of **leukotriene**, for treating rhinitis/conjunctivitis)

IT Drug delivery systems
(nasal; **combination** of non-sedative anti-**histamines** contg. substances which influence action of **leukotriene**, for treating rhinitis/conjunctivitis)

IT Drug delivery systems
(ophthalmic; **combination** of non-sedative anti-**histamines** contg. substances which influence action of **leukotriene**, for treating rhinitis/conjunctivitis)

IT Drug delivery systems
(oral; **combination** of non-sedative anti-**histamines** contg. substances which influence action of **leukotriene**, for treating rhinitis/conjunctivitis)

IT **Nose**
(rhinitis; **combination** of non-sedative anti-**histamines** contg. substances which influence action of **leukotriene**, for treating rhinitis/conjunctivitis)

IT Drug delivery systems
(topical; **combination** of non-sedative anti-**histamines** contg. substances which influence action of **leukotriene**, for treating rhinitis/conjunctivitis)

IT 73836-78-9, **Leukotriene** D4
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(antagonist; **combination** of non-sedative anti-**histamines** contg. substances which influence action of **leukotriene**, for treating rhinitis/conjunctivitis)

IT 79307-93-0, Azelastine hydrochloride **158966-92-8**, **Montelukast** 197584-39-7, AWD 23-115
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**combination** of non-sedative anti-**histamines** contg. substances which influence action of **leukotriene**, for treating rhinitis/conjunctivitis)

IT **68844-77-9**, **Astemizole** 79516-68-0, Levocabastine 79672-88-1, Piriprost **83799-24-0**, **Fexofenadine** **83881-51-0**, **Cetirizine** 103177-37-3, Pranlukast 107753-78-6, Zafirlukast 108612-45-9, Mizolastine 111406-87-2, Zileuton 118414-82-7, MK-886 128253-31-6, Bay x 1005 147030-01-1, MK-591
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**combination** of non-sedative anti-**histamines** contg. substances which influence action of **leukotriene**, for treating rhinitis/conjunctivitis)

IT 79794-75-5, **Loratadine**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**combination** of non-sedative anti-**histamines** with the exception of **loratadine**-type compds. contg. substances

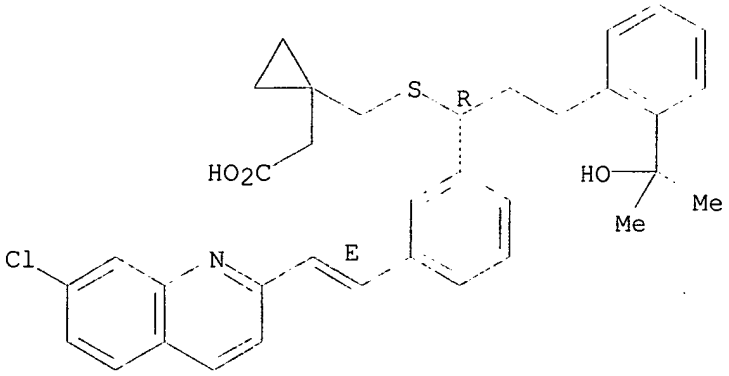
which influence action of **leukotriene**, for treating rhinitis/conjunctivitis)

IT 80619-02-9, 5-Lipoxygenase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(inhibitor; **combination** of non-sedative anti-**histamines** contg. substances which influence action of **leukotriene**, for treating rhinitis/conjunctivitis)

IT **158966-92-8, Montelukast**
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**combination** of non-sedative anti-**histamines** contg. substances which influence action of **leukotriene**, for treating rhinitis/conjunctivitis)

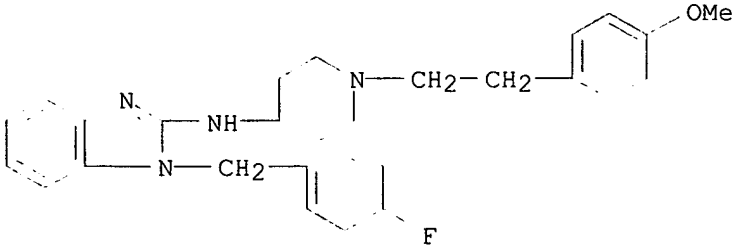
RN 158966-92-8 HCAPLUS
CN Cyclopropaneacetic acid, 1-[[[(1R)-1-[3-[(1E)-2-(7-chloro-2-quinolinyl)ethenyl]phenyl]-3-[2-(1-hydroxy-1-methylethyl)phenyl]propyl]thio]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

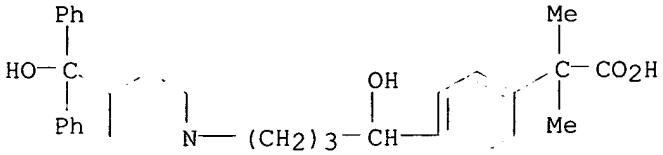


IT **68844-77-9, Astemizole 83799-24-0, Fexofenadine 83881-51-0, Cetirizine**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**combination** of non-sedative anti-**histamines** contg. substances which influence action of **leukotriene**, for treating rhinitis/conjunctivitis)

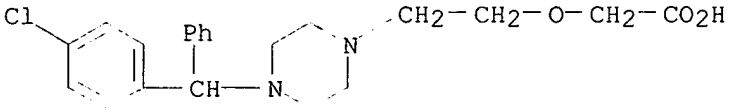
RN 68844-77-9 HCAPLUS
CN 1H-Benzimidazol-2-amine, 1-[(4-fluorophenyl)methyl]-N-[1-[2-(4-methoxyphenyl)ethyl]-4-piperidinyl]- (9CI) (CA INDEX NAME)



RN 83799-24-0 HCAPLUS
CN Benzeneacetic acid, 4-[1-hydroxy-4-[4-(hydroxydiphenylmethyl)-1-piperidinyl]butyl]-.alpha.,.alpha.-dimethyl- (9CI) (CA INDEX NAME)



RN 83881-51-0 HCAPLUS
CN Acetic acid, [2-[4-[(4-chlorophenyl)phenylmethyl]-1-piperazinyl]ethoxy]- (9CI) (CA INDEX NAME)



L89 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2003 ACS
AN **2001:79915** HCAPLUS
DN **135:131511**
TI Present and potential therapy for allergic rhinitis. A review
AU Reichmuth, Daniel; Lockey, Richard F.
CS Division of Allergy and Immunology, University of South Florida College of Medicine, Tampa, FL, USA
SO BioDrugs (**2000**), 14(6), 371-387
CODEN: BIDRF4; ISSN: 1173-8804
PB Adis International Ltd.
DT Journal; General Review
LA English
CC 1-0 (Pharmacology)
Section cross-reference(s): 2, 15
AB A review with 160 refs. Allergic rhinitis can affect up to one-fifth of the population and the economic impact is increasing. H1 receptor antagonists were the first major pharmacol. treatment, but the assocd. sedation limited their use. The 2 initial second generation less sedating **antihistamines**, **astemizole** and terfenadine, were found to prolong the cardiac QTc interval, esp. when administered with other medications metabolized by the same cytochrome (CYP) P 450 isoenzyme, CYP3A4. Other second generation **antihistamines**, **fexofenadine**, **loratadine** and **cetirizine**, do not cause clin. significant cardiac QTc interval prolongation. Two newer agents, **ebastine** and mizolastine, are also effective in the treatment of allergic rhinitis. **Ebastine**, however, prolongs the cardiac QTc interval in lab. animals and humans, the clin. significance of which is unknown. **Desloratadine** and **norastemizole**, metabolites of **loratadine** and **astemizole**, resp., are 2 other second generation **antihistamines** found to be effective treatments for seasonal allergic rhinitis. Unlike their parent compds., they do not prolong the cardiac QTc interval. All clin. available intranasal corticosteroids are effective in the treatment of allergic rhinitis, but studies to evaluate possible long term systemic adverse effects are limited. Mometasone furoate and fluticasone propionate have lower oral bioavailability compared with other corticosteroids that are given intranasally. This may be important, since it is likely that some of the intranasal corticosteroid is ingested. Two 1-yr growth studies in children indicated that intranasal beclomethasone dipropionate given twice daily reduces growth velocity, whereas intranasal mometasone furoate given once daily in the morning does not. Other studies are needed. Most but not all studies have shown that **leukotriene** antagonists are

effective in the treatment of allergic rhinitis. H1 receptor antagonists are not very effective in reducing nasal congestion, but **leukotriene** antagonists do attenuate this symptom. Furthermore, one study demonstrates an additive benefit in treating allergic rhinitis with the **combination** of a H1 receptor and **leukotriene** antagonist. Clin. trials have demonstrated that anti-Ig (Ig) E is effective in the treatment of seasonal allergic rhinitis when free IgE is reduced to <25 .mu.g/L. The redn. of total IgE is dose dependent and s.c. and i.v. administration are both effective. Immunotherapy is also an effective treatment for allergic rhinitis. CpG oligonucleotides is a novel adjuvant for allergen immunotherapy. This adjuvant used in a murine model shifts the immune response away from the allergic or TH2 phenotype. Studies in humans have not been performed.

ST review **antihistamine leukotriene** antagonist immunotherapy allergic rhinitis

IT **Antihistamines**
(**H1**; present and potential therapy for allergic rhinitis in humans)

IT **Antihistamines**
Hay fever
Immunotherapy
Leukotriene antagonists
(present and potential therapy for allergic rhinitis in humans)

IT Corticosteroids, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(present and potential therapy for allergic rhinitis in humans)

IT 50679-08-8, Terfenadine **68844-77-9, Astemizole 90729-43-4, Ebastine**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(present and potential therapy for allergic rhinitis in humans)

IT **75970-99-9, Norastemizole** 79794-75-5, **Loratadine** 80474-14-2, Fluticasone propionate **83799-24-0, Fexofenadine 83881-51-0, Cetirizine** 83919-23-7, Mometasone furoate **100643-71-8, Desloratadine** 108612-45-9, Mizolastine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(present and potential therapy for allergic rhinitis in humans)

IT 5534-09-8, Beclomethasone dipropionate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(present and potential therapy for allergic rhinitis in humans)

RE.CNT 160 THERE ARE 160 CITED REFERENCES AVAILABLE FOR THIS RECORD

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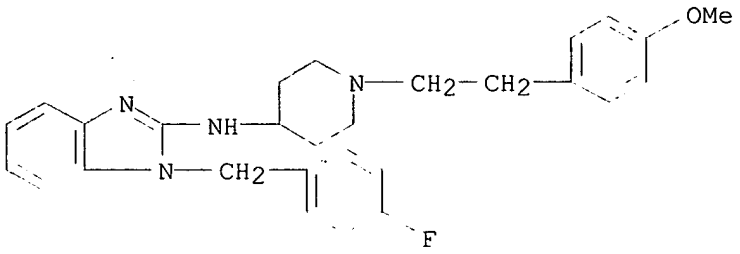
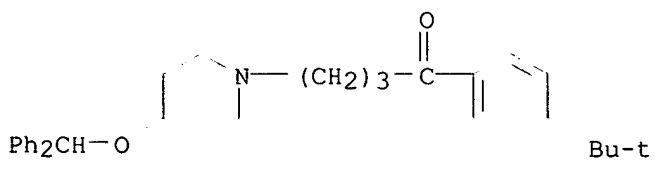
IT **68844-77-9, Astemizole 90729-43-4, Ebastine**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(present and potential therapy for allergic rhinitis in humans)

RN 68844-77-9 HCAPLUS
CN 1H-Benzimidazol-2-amine, 1-[(4-fluorophenyl)methyl]-N-[1-[2-(4-methoxyphenyl)ethyl]-4-piperidinyl]- (9CI) (CA INDEX NAME)

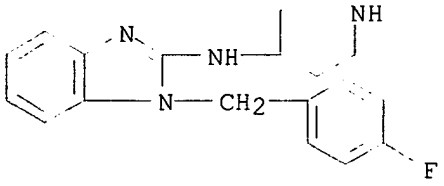


RN 90729-43-4 HCAPLUS
CN 1-Butanone, 1-[4-(1,1-dimethylethyl)phenyl]-4-[4-(diphenylmethoxy)-1-piperidinyl]- (9CI) (CA INDEX NAME)

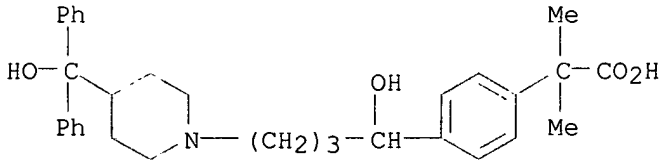


IT **75970-99-9, Norastemizole 83799-24-0, Fexofenadine 83881-51-0, Cetirizine 100643-71-8, Desloratadine**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(present and potential therapy for allergic rhinitis in humans)

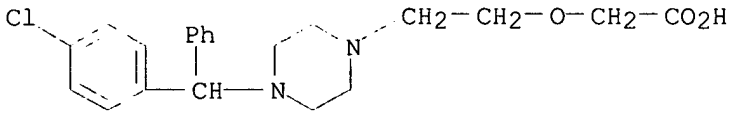
RN 75970-99-9 HCAPLUS
CN 1H-Benzimidazol-2-amine, 1-[(4-fluorophenyl)methyl]-N-4-piperidinyl- (9CI) (CA INDEX NAME)



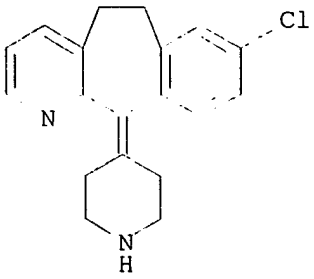
RN 83799-24-0 HCAPLUS
CN Benzeneacetic acid, 4-[1-hydroxy-4-[4-(hydroxydiphenylmethyl)-1-piperidinyl]butyl]-.alpha.,.alpha.-dimethyl- (9CI) (CA INDEX NAME)



RN 83881-51-0 HCAPLUS
CN Acetic acid, [2-[4-[(4-chlorophenyl)phenylmethyl]-1-piperazinyl]ethoxy]- (9CI) (CA INDEX NAME)



RN 100643-71-8 HCAPLUS
CN 5H-Benzo[5,6]cyclohepta[1,2-b]pyridine, 8-chloro-6,11-dihydro-11-(4-piperidinylidene)- (9CI) (CA INDEX NAME)



L89 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2003 ACS
AN **1999:672612** HCAPLUS
DN **131:303379**
TI Methods and **compositions** using **norastemizole** in **combination** with **leukotriene** inhibitors
IN Rubin, Paul D.
PA Sepracor Inc., USA
SO PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K045-06
CC 63-6 (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9952555	A1	19991021	WO 1999-US8078	19990413 <--
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6248308	B1	20010619	US 1998-59572	19980414 <--
	CA 2328075	AA	19991021	CA 1999-2328075	19990413 <--
	AU 9935581	A1	19991101	AU 1999-35581	19990413 <--
	EP 1071462	A1	20010131	EP 1999-917464	19990413 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2002511427	T2	20020416	JP 2000-543165	19990413 <--
	US 6372197	B1	20020416	US 2000-721668	20001127 <--
	US 2002086854	A1	20020704	US 2002-84250	20020228 <--
PRAI	US 1998-59572	A	19980414 <--		
	WO 1999-US8078	W	19990413 <--		
	US 2000-721668	A3	20001127		

AB Methods and pharmaceutical **compns.** employing **norastemizole** and a **leukotriene** inhibitor for the treatment or prevention of inflammation or allergic disorders, such as asthma or the symptoms thereof. Also included are methods and **compns.** employing **norastemizole** and a decongestant for the treatment or prevention of inflammation or allergic disorders, such as asthma or the symptoms thereof.

ST **norastemizole leukotriene** inhibitor **combination** pharmaceutical

IT Allergy inhibitors
Antiasthmatics
Antihistamines
Decongestants
(pharmaceuticals contg. **norastemizole** in **combination** with **leukotriene** inhibitors)

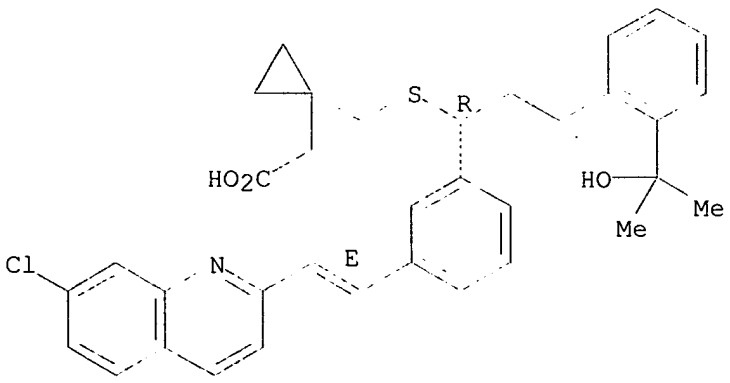
IT **Leukotriene antagonists**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceuticals contg. **norastemizole** in **combination** with **leukotriene** inhibitors)

IT Drug delivery systems
(solids, oral; pharmaceuticals contg. **norastemizole** in **combination** with **leukotriene** inhibitors)

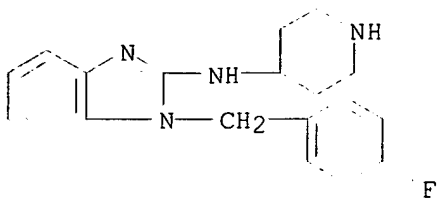
IT Drug delivery systems
(sprays; pharmaceuticals contg. **norastemizole** in **combination** with **leukotriene** inhibitors)

IT 80619-02-9, 5-Lipoxygenase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; pharmaceuticals contg. **norastemizole** in **combination** with **leukotriene** inhibitors)
IT 103177-37-3, Pranlukast 107753-78-6, Zafirlukast **158966-92-8, Montelukast** 171031-57-5 247016-81-5
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (**leukotriene** antagonist; pharmaceuticals contg. **norastemizole** in **combination** with **leukotriene** inhibitors)
IT 79672-88-1, Piriprost 80809-81-0, Docebenone 111406-87-2, Zileuton 118414-82-7, MK-886 140841-32-3 147030-01-1, MK-591
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (lipoxygenase inhibitor; pharmaceuticals contg. **norastemizole** in **combination** with **leukotriene** inhibitors)
IT **75970-99-9, Norastemizole**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (pharmaceuticals contg. **norastemizole** in **combination** with **leukotriene** inhibitors)
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Henk, T; US 5714501 A 1998 HCAPLUS
(2) Procter & Gamble; WO 9746243 A 1997 HCAPLUS
(3) Schering Corp; WO 9932125 A 1999 HCAPLUS
IT **158966-92-8, Montelukast**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (**leukotriene** antagonist; pharmaceuticals contg. **norastemizole** in **combination** with **leukotriene** inhibitors)
RN 158966-92-8 HCAPLUS
CN Cyclopropaneacetic acid, 1-[[[(1R)-1-[3-[(1E)-2-(7-chloro-2-quinolinyl)ethenyl]phenyl]-3-[2-(1-hydroxy-1-methylethyl)phenyl]propyl]thio]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IT **75970-99-9, Norastemizole**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (pharmaceuticals contg. **norastemizole** in **combination** with **leukotriene** inhibitors)
RN 75970-99-9 HCAPLUS
CN 1H-Benzimidazol-2-amine, 1-[(4-fluorophenyl)methyl]-N-4-piperidinyl- (9CI) (CA INDEX NAME)



L89 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2003 ACS
AN **1999:672609** HCAPLUS
DN **131:303378**
TI Methods and **compositions** using **cetirizine** in **combination** with **leukotriene** inhibitors for treating conditions responsive to **leukotriene** inhibition
IN Rubin, Paul D.
PA Sepracor Inc., USA
SO PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K045-06
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 28
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9952553	A1	19991021	WO 1999-US8076	19990413 <--
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6384038	B1	20020507	US 1998-59571	19980414 <--
	CA 2328073	AA	19991021	CA 1999-2328073	19990413 <--
	AU 9935580	A1	19991101	AU 1999-35580	19990413 <--
	EP 1071461	A1	20010131	EP 1999-917463	19990413 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2002511425	T2	20020416	JP 2000-543163	19990413 <--
	US 2002099058	A1	20020725	US 2002-105331	20020326 <--
PRAI	US 1998-59571	A	19980414 <--		
	WO 1999-US8076	W	19990413 <--		

AB Methods and pharmaceutical **compns.** employ (+)-, (-)-, or (.+-.)-**cetirizine**, or a pharmaceutically acceptable salt thereof, and a **leukotriene** inhibitor, or a pharmaceutically acceptable salt thereof, or decongestant for the treatment, management, and/or prevention of inflammation, asthma or symptoms thereof, allergic disorders such as allergic rhinitis, and dermatitis. (+)- And (-)-**cetirizine**-2HCl were prepd. by hydrolysis of the corresponding (-)- and (+)- acetonitrile derivs.
ST **cetirizine** pharmaceutical **leukotriene** inhibitor
IT Allergy inhibitors
Anti-inflammatory agents
Antiasthmatics
(prepn. of **cetirizine** enantiomers for use in **combination** with **leukotriene** inhibitors for treating

conditions responsive to **leukotriene** inhibition)

IT **Leukotriene antagonists**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of **cetirizine** enantiomers for use in **combination** with **leukotriene** inhibitors for treating conditions responsive to **leukotriene** inhibition)

IT 80619-02-9, 5-Lipoxygenase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; prepn. of **cetirizine** enantiomers for use in **combination** with **leukotriene** inhibitors for treating conditions responsive to **leukotriene** inhibition)

IT 79672-88-1, Piriprost 80809-81-0, Docebenone 111406-87-2, Zileuton 118414-82-7, MK-886 140841-32-3, ICI-D2138 147030-01-1, MK-591
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(lipoxygenase inhibitor; prepn. of **cetirizine** enantiomers for use in **combination** with **leukotriene** inhibitors for treating conditions responsive to **leukotriene** inhibition)

IT 841-77-0, 1-(Diphenylmethyl)piperazine 36961-64-5, 2-(2-Chloroethoxy)acetamide 130018-75-6, Acetonitrile, [2-[4-[(4-chlorophenyl)phenylmethyl]-1-piperazinyl]ethoxy]-
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of **cetirizine** enantiomers for use in **combination** with **leukotriene** inhibitors for treating conditions responsive to **leukotriene** inhibition)

IT 83881-35-0P 130018-78-9P, Acetonitrile, [2-[4-[(4-chlorophenyl)phenylmethyl]-1-piperazinyl]ethoxy]-, (-)- 130018-90-5P, (+)-1-[(4-Chlorophenyl)phenylmethyl]piperazine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of **cetirizine** enantiomers for use in **combination** with **leukotriene** inhibitors for treating conditions responsive to **leukotriene** inhibition)

IT **83881-51-0P, Cetirizine 83881-52-1P**, Acetic acid, [2-[4-[(4-chlorophenyl)phenylmethyl]-1-piperazinyl]ethoxy]-, dihydrochloride 130018-76-7P, Acetic acid, [2-[4-[(4-chlorophenyl)phenylmethyl]-1-piperazinyl]ethoxy]-, (S)- 130018-77-8P, Acetic acid, [2-[4-[(4-chlorophenyl)phenylmethyl]-1-piperazinyl]ethoxy]-, (R)- 130018-87-0P 163837-48-7P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of **cetirizine** enantiomers for use in **combination** with **leukotriene** inhibitors for treating conditions responsive to **leukotriene** inhibition)

IT 103177-37-3, Pranlukast 107753-78-6, Zafirlukast **158966-92-8, Montelukast** 171031-57-5 247016-81-5
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of **cetirizine** enantiomers for use in **combination** with **leukotriene** inhibitors for treating conditions responsive to **leukotriene** inhibition)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD

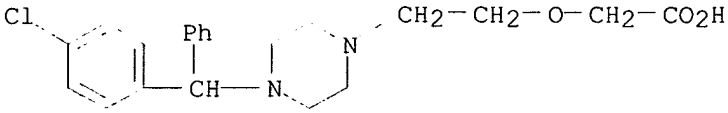
RE

(1) Da Motta; BRITISH JOURNAL OF PHARMACOLOGY 1994, V112(1), P111 MEDLINE
(2) Procter & Gamble; EP 0780127 A 1997 HCAPLUS
(3) Schering Corp; WO 9932125 A 1999 HCAPLUS

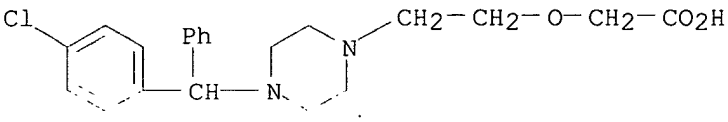
IT **83881-51-0P, Cetirizine 83881-52-1P**, Acetic acid, [2-[4-[(4-chlorophenyl)phenylmethyl]-1-piperazinyl]ethoxy]-, dihydrochloride
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of **cetirizine** enantiomers for use in **combination** with **leukotriene** inhibitors for treating conditions responsive to **leukotriene** inhibition)

RN 83881-51-0 HCAPLUS

CN Acetic acid, [2-[4-[(4-chlorophenyl)phenylmethyl]-1-piperazinyl]ethoxy]- (9CI) (CA INDEX NAME)



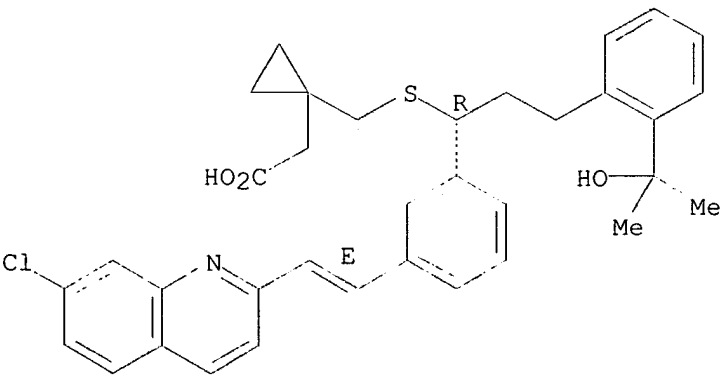
RN 83881-52-1 HCAPLUS
CN Acetic acid, [2-[4-[(4-chlorophenyl)phenylmethyl]-1-piperazinyl]ethoxy]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

IT **158966-92-8, Montelukast**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of **cetirizine** enantiomers for use in **combination** with **leukotriene** inhibitors for treating conditions responsive to **leukotriene** inhibition)
RN 158966-92-8 HCAPLUS
CN Cyclopropaneacetic acid, 1-[[[(1R)-1-[3-[(1E)-2-(7-chloro-2-quinolinyl)ethenyl]phenyl]-3-[2-(1-hydroxy-1-methylethyl)phenyl]propyl]thio]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L89 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2003 ACS
AN **1999:425758** HCAPLUS
DN **131:63456**
TI **Composition** for treating respiratory and skin diseases, **comprising** at least one **leukotriene** antagonist and at least one **antihistamine**
IN Jensen, Peder K.; Lorber, Richard R.; Danzig, Melvyn R.; **Medeiros, Paul T.**

PA **Schering Corporation, USA**
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-55
ICS A61K031-495; A61K031-47; A61K031-445
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9932125	A1	19990701	WO 1998-US26223	19981221 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MD, MG, MK, MN, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	ZA 9811731	A	19990621	ZA 1998-11731	19981221 <--
	CA 2315721	AA	19990701	CA 1998-2315721	19981221 <--
	AU 9919071	A1	19990712	AU 1999-19071	19981221 <--
	BR 9814417	A	20001010	BR 1998-14417	19981221 <--
	EP 1041990	A1	20001011	EP 1998-963828	19981221 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, LT, LV, FI, RO				
	JP 2001526232	T2	20011218	JP 2000-525116	19981221 <--
	NO 2000003288	A	20000822	NO 2000-3288	20000622 <--

PRAI US 1997-68638P P 19971223 <--
US 1998-78638P P 19980319 <--
WO 1998-US26223 W 19981221 <--

AB The invention relates to a pharmaceutical **compn.** useful in the treatment of sneezing, itching runny nose, nasal congestion, redness of the eye, tearing, itching of the ears or palate, shortness of breath, inflammation of the bronchial mucosa, reduced Forced Expiratory Vol. In One Second (FEV1), coughs, rash, itchy skin, headaches, and aches and pains assocd. with seasonal allergic rhinitis, perennial allergic rhinitis, common colds, otitis, sinusitus, allergy, asthma, allergic asthma and/or inflammation, in a mammalian organism in need of such treatment. The **compn. comprises**: (i) an effective amt. of at least one **leukotriene** antagonist selected from (a) **montelukast**, (b) 1-(((R)- (3-(2-(6,7- difluoro-2-quinolinyl)ethenyl)phenyl)-3-(2- (2-hydroxy-2-propyl)phenyl)propyl) thio)methylcyclopropaneacetic acid; (c) 1-(((1(R)-3 (3-(2-(2,3-dichlorothieno[3, 2-b]pyridin-5-yl) -(E)-ethenyl)phenyl) -3-(2-(1-hydroxy-1- methylethyl) phenyl)propyl) thio)methyl) cyclopropaneacetic acid; (d) pranlukast; or (f) [2-[[2-(4-tert -butyl-2-thiazolyl) -5-benzofuranyl] oxymethyl]phenyl] acetic acid; or a pharmaceutically acceptable salt thereof; in **admixt.** with (ii) an effective amt. of at least one **antihistamine** which is **descarboethoxyloratidine, cetirizine, fexofenadine, ebastine, astemizole, norastemizole, epinastine, efletirizine** or a pharmaceutically acceptable salt thereof.

ST capsule **leukotriene** antagonist **antihistamine**; respiratory skin disease **leukotriene** antagonist **antihistamine**

IT Drug delivery systems
(capsules; **compn.** for treating respiratory and skin diseases, **comprising** at least one **leukotriene** antagonist and at least one **antihistamine**)

IT Analgesics
Antihistamines
Antitussives
Decongestants
Drug delivery systems
Expectorants
Skin, disease
(**compn.** for treating respiratory and skin diseases, **comprising** at least one **leukotriene** antagonist and at least one **antihistamine**)

IT **Leukotriene antagonists**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**compn.** for treating respiratory and skin diseases, **comprising** at least one **leukotriene** antagonist and at least one **antihistamine**)

IT **Respiratory tract**
(disease; **compn.** for treating respiratory and skin diseases, **comprising** at least one **leukotriene** antagonist and at least one **antihistamine**)

IT Drug delivery systems
(gels; **compn.** for treating respiratory and skin diseases, **comprising** at least one **leukotriene** antagonist and at least one **antihistamine**)

IT Drug delivery systems
(powders; **compn.** for treating respiratory and skin diseases, **comprising** at least one **leukotriene** antagonist and at least one **antihistamine**)

IT Drug delivery systems
(tablets; **compn.** for treating respiratory and skin diseases, **comprising** at least one **leukotriene** antagonist and at least one **antihistamine**)

IT 90-82-4, Pseudoephedrine 93-14-1, Guaifenesin 125-71-3, Dextromethorphan **68844-77-9, Astemizole 75970-99-9, Norastemizole 80012-43-7, Epinastine 83799-24-0, Fexofenadine 83881-51-0, Cetirizine 90729-43-4, Ebastine 100643-71-8** 103177-37-3, Pranlukast 107753-78-6, Zafirlukast 149413-74-1 **150756-35-7, Efletirizine** 152952-65-3 **158966-92-8, Montelukast** 172927-32-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**compn.** for treating respiratory and skin diseases, **comprising** at least one **leukotriene** antagonist and at least one **antihistamine**)

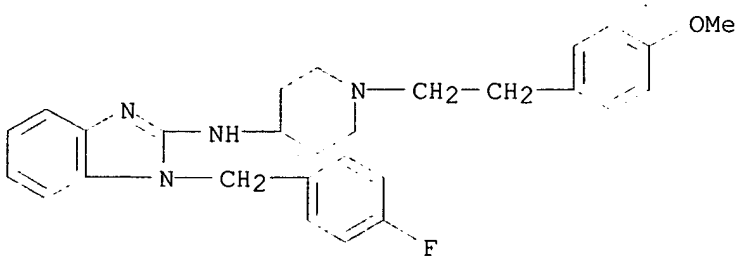
RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Allergan Inc; WO 9303723 A 1993 HCAPLUS
(2) Boehringer Ingelheim KG; DE 4203201 A 1993
(3) Dahlen, S; WO 9728797 A 1997 HCAPLUS
(4) Merck Frosst Canada Inc; EP 0565185 A 1993 HCAPLUS
(5) Procter & Gamble; EP 0780127 A 1997 HCAPLUS
(6) Procter & Gamble; WO 9746243 A 1997 HCAPLUS
(7) Sepracor Inc; WO 9834611 A 1998 HCAPLUS
(8) Warner Lambert Co; WO 9848839 A 1998 HCAPLUS

IT **68844-77-9, Astemizole 75970-99-9, Norastemizole 80012-43-7, Epinastine 83799-24-0, Fexofenadine 83881-51-0, Cetirizine 90729-43-4, Ebastine 100643-71-8 150756-35-7, Efletirizine 158966-92-8, Montelukast**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**compn.** for treating respiratory and skin diseases, **comprising** at least one **leukotriene** antagonist and at

least one **antihistamine**)

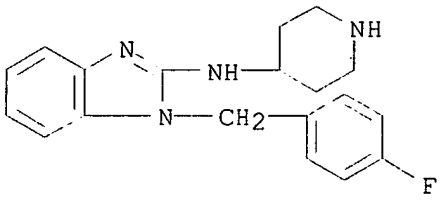
RN 68844-77-9 HCAPLUS

CN 1H-Benzimidazol-2-amine, 1-[(4-fluorophenyl)methyl]-N-[1-[2-(4-methoxyphenyl)ethyl]-4-piperidinyl]- (9CI) (CA INDEX NAME)



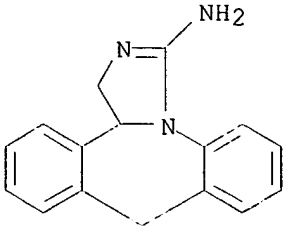
RN 75970-99-9 HCAPLUS

CN 1H-Benzimidazol-2-amine, 1-[(4-fluorophenyl)methyl]-N-4-piperidinyl- (9CI) (CA INDEX NAME)



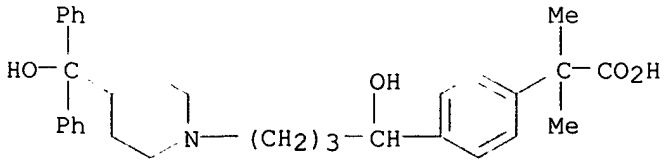
RN 80012-43-7 HCAPLUS

CN 1H-Dibenz[c,f]imidazo[1,5-a]azepin-3-amine, 9,13b-dihydro- (9CI) (CA INDEX NAME)



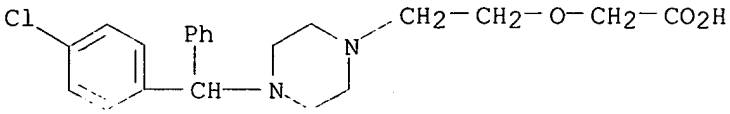
RN 83799-24-0 HCAPLUS

CN Benzeneacetic acid, 4-[1-hydroxy-4-[4-(hydroxydiphenylmethyl)-1-piperidinyl]butyl]-.alpha.,.alpha.-dimethyl- (9CI) (CA INDEX NAME)

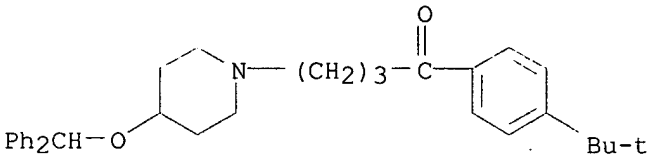


RN 83881-51-0 HCAPLUS

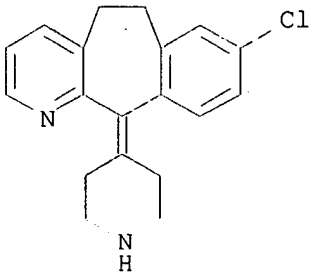
CN Acetic acid, [2-[4-[(4-chlorophenyl)phenylmethyl]-1-piperazinyl]ethoxy]- (9CI) (CA INDEX NAME)



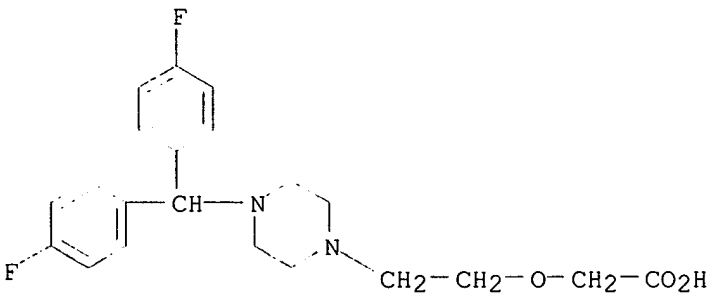
RN 90729-43-4 HCAPLUS
CN 1-Butanone, 1-[4-(1,1-dimethylethyl)phenyl]-4-[4-(diphenylmethoxy)-1-piperidinyl]- (9CI) (CA INDEX NAME)



RN 100643-71-8 HCAPLUS
CN 5H-Benzo[5,6]cyclohepta[1,2-b]pyridine, 8-chloro-6,11-dihydro-11-(4-piperidinylidene)- (9CI) (CA INDEX NAME)

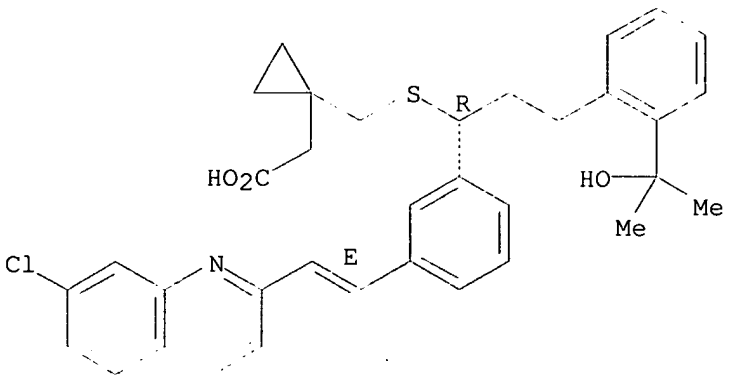


RN 150756-35-7 HCAPLUS
CN Acetic acid, [2-[4-[bis(4-fluorophenyl)methyl]-1-piperazinyl]ethoxy]- (9CI) (CA INDEX NAME)



RN 158966-92-8 HCAPLUS
CN Cyclopropaneacetic acid, 1-[[[(1R)-1-[3-[(1E)-2-(7-chloro-2-quinolinyl)ethenyl]phenyl]-3-[2-(1-hydroxy-1-methylethyl)phenyl]propyl]thio]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L89 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2003 ACS
AN **1998:548530** HCAPLUS
DN **129:156932**
TI Treatment of allergic asthma and other disorders with **descarboethoxyloratadine**
IN Handley, Dean A.; Rubin, Paul D.
PA Sepracor, Inc., USA
SO PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-44
CC 1-7 (Pharmacology)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9834611	A1	19980813	WO 1998-US2564	19980210 <--
	W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, GW, HU, ID, IL, IS, JP, KG, KP, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5900421	A	19990504	US 1997-799605	19970211 <--
	AU 9864348	A1	19980826	AU 1998-64348	19980210 <--
	AU 719907	B2	20000518		
	BR 9807673	A	20000215	BR 1998-7673	19980210 <--
	EP 1005345	A1	20000607	EP 1998-909996	19980210 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2002514202	T2	20020514	JP 1998-535015	19980210 <--
	US 5962464	A	19991005	US 1998-110367	19980706 <--
	US 6054463	A	20000425	US 1999-271269	19990317 <--
	NO 9903847	A	19990927	NO 1999-3847	19990810 <--
	US 2002040034	A1	20020404	US 2000-556699	20000424 <--
PRAI	US 1997-799605	A	19970211 <--		
	WO 1998-US2564	W	19980210 <--		
	US 1998-110367	A1	19980706 <--		
	US 1999-271269	A1	19990317 <--		

AB Methods utilizing **descarboethoxyloratadine** (I), for the treatment of allergic disorders, while avoiding the **concomitant** liability of adverse side-effects assocd. with other non-sedating **antihistamines** are disclosed. Also included are methods for the treatment of allergic asthma using I and either a decongestant or a **leukotriene** inhibitor, while avoiding the **concomitant** liability of adverse side-effects assocd. with other non-sedating

antihistamines. The invention also encompasses the administration of I in a nasal or oral spray. A capsule contained I 0.1, lactose 150, cellulose 50, and magnesium stearate 6 mg.

ST allergic asthma treatment **descarboethoxyloratadine** pharmaceutical capsule

IT Asthma
(allergic, inhibitors; treatment of allergic asthma and other disorders with **descarboethoxyloratadine**)

IT **Heart, disease**
(**arrhythmia**; treatment of allergic asthma and other disorders with **descarboethoxyloratadine**)

IT Drug delivery systems
(capsules; treatment of allergic asthma and other disorders with **descarboethoxyloratadine**)

IT Drug delivery systems
(nasal sprays; treatment of allergic asthma and other disorders with **descarboethoxyloratadine**)

IT Drug delivery systems
(sprays, oral; treatment of allergic asthma and other disorders with **descarboethoxyloratadine**)

IT Drug delivery systems
(tablets; treatment of allergic asthma and other disorders with **descarboethoxyloratadine**)

IT **Antihistamines**
Decongestants
Neoplasm
(treatment of allergic asthma and other disorders with **descarboethoxyloratadine**)

IT **Leukotriene antagonists**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of allergic asthma and other disorders with **descarboethoxyloratadine**)

IT 73836-78-9, **Leukotriene** d4
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; treatment of allergic asthma and other disorders with **descarboethoxyloratadine**)

IT 80619-02-9, 5-Lipoxygenase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; treatment of allergic asthma and other disorders with **descarboethoxyloratadine**)

IT **100643-71-8, Descarboethoxyloratadine**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of allergic asthma and other disorders with **descarboethoxyloratadine**)

IT 9035-51-2, Cytochrome p450, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(treatment of allergic asthma and other disorders with **descarboethoxyloratadine**)

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

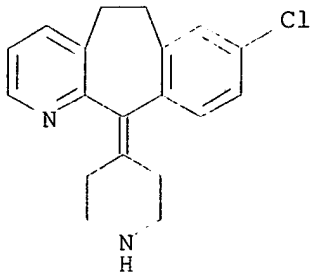
(1) Aberg; US 5595997 A 1997 HCAPLUS

(2) Piwinski; US 5089496 A 1992 HCAPLUS

IT **100643-71-8, Descarboethoxyloratadine**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of allergic asthma and other disorders with **descarboethoxyloratadine**)

RN 100643-71-8 HCAPLUS

CN 5H-Benzo[5,6]cyclohepta[1,2-b]pyridine, 8-chloro-6,11-dihydro-11-(4-piperidinylidene)- (9CI) (CA INDEX NAME)



=> d all tot

L94 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2003 ACS
AN 1998:719296 HCAPLUS
DN 129:347313
TI Topical nasal antiinflammatory **compositions**
IN Segal, Catherine A.
PA Warner-Lambert Co., USA
SO PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K045-06
ICS A61K031-57; A61K031-58; A61K031-135; A61K031-35; A61K031-245; A61K031-09; A61K031-38; A61K031-195; A61K031-47; A61K031-445; A61K031-55; A61K031-44; A61K031-615; A61K031-415
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9848839	A1	19981105	WO 1998-US6483	19980402 <--
	W: AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, GW, HU, ID, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9868780	A1	19981124	AU 1998-68780	19980402 <--
	EP 979105	A1	20000216	EP 1998-914420	19980402 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	BR 9809022	A	20000801	BR 1998-9022	19980402 <--
	JP 2001524108	T2	20011127	JP 1998-546998	19980402 <--
PRAI	US 1997-44306P	P	19970430 <--		
	WO 1998-US6483	W	19980402 <--		

AB Topically applicable nasal **compns. comprise** a therapeutically effective amt. of an antiinflammatory agent and a at least one agent selected from the group consisting of a vasoconstrictor, a neuramidinase inhibitor, a leukotriene inhibitor, an antihistamine, an antiallergic agent, an anticholinergic agent, an anesthetic and a mucolytic agent. The present **compns.** are useful as nasal sprays and nose drops for the treatment of nasal and sinus conditions.
ST topical nasal antiinflammatory; vasoconstrictor topical nasal

antiinflammatory; antihistamine topical nasal antiinflammatory; antiallergic topical nasal antiinflammatory
IT Drug delivery systems
(nasal sprays; topical nasal antiinflammatory **compns**.)
IT Drug delivery systems
(nasal; topical nasal antiinflammatory **compns**.)
IT Drug delivery systems
Drug delivery systems
(solns., nasal; topical nasal antiinflammatory **compns**.)
IT Allergy inhibitors
Anesthetics
Anti-inflammatory agents
Antihistamines
Cholinergic antagonists
Expectorants
Humectants
Vasoconstrictors
(topical nasal antiinflammatory **compns**.)
IT **Leukotriene antagonists**
Polyoxyalkylenes, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(topical nasal antiinflammatory **compns**.)
IT 9001-67-6, Neuraminidase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; topical nasal antiinflammatory **compns**.)
IT 50-02-2, Dexamethasone 56-81-5, Glycerin, biological studies 57-55-6, Propylene glycol, biological studies 58-73-1, Diphenhydramine 59-42-7, Phenylephrine 76-25-5, Triamcinolone acetonide 93-14-1, Guaifenesin 94-09-7, Benzocaine 113-92-8 140-65-8, Pramoxine 526-36-3, Xylometazoline 586-60-7, Dyclonine 616-91-1, Acetylcysteine 835-31-4, Naphazoline 1491-59-4, Oxymetazoline 3964-81-6, Azatadine 5534-09-8, Beclomethasone dipropionate 15826-37-6, Cromolyn sodium 22254-24-6, Ipratropium bromide 25322-68-3, PEG 50679-08-8, Terfenadine 51333-22-3, Budesonide 58581-89-8, Azelastine 60205-81-4, Ipratropium **68844-77-9**, **Astemizole** 69049-73-6, Nedocromil **75970-99-9**, **Norastemizole** 79516-68-0, Levocabastine 80474-14-2, Fluticasone propionate **83799-24-0**, **Fexofenadine 83881-51-0**, **Cetirizine** 83919-23-7, Mometasone furoate 107753-78-6, Zafirlukast 111406-87-2, Zileuton 139110-80-8, Zanamivir
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(topical nasal antiinflammatory **compns**.)
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Bayer Ag; WO 9709067 A 1997 HCAPLUS
(2) Bollinger, F; US 3482015 A 1969
(3) Center For Innovative Technology; WO 9309764 A 1993 HCAPLUS
(4) McNeil-Ppc Inc; WO 9701337 A 1997 HCAPLUS
(5) McNeil-Ppc Inc; WO 9701341 A 1997 HCAPLUS
(6) Sekisui Chem Ind Co Ltd; JP 62153227 A 1987 HCAPLUS
(7) Stevenson, N; US 4053628 A 1977 HCAPLUS
(8) Sunshine; WO 8504589 A 1985 HCAPLUS
(9) The Procter & Gamble Company; WO 9507103 A 1995 HCAPLUS
(10) The Procter & Gamble Company; EP 0780127 A 1997 HCAPLUS

L94 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2003 ACS
AN 1997:812193 HCAPLUS
DN 128:80034
TI A nasal spray containing an intranasal steroid and an antihistamine
IN Koochaki, Patricia Elaine
PA Procter & Gamble Company, USA
SO PCT Int. Appl., 17 pp.
CODEN: PIXXD2

DT Patent
LA English
IC ICM A61K031-57
ICS A61K031-56; A61K031-44; A61K031-445; A61K031-415; A61K031-57; A61K031-44; A61K031-57; A61K031-44; A61K031-445; A61K031-57; A61K031-44; A61K031-415
CC 63-6 (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9746243	A1	19971211	WO 1997-US9518	19970603 <--
	W: AU, BR, CA, CN, JP, MX				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9731537	A1	19980105	AU 1997-31537	19970603
	CN 1222852	A	19990714	CN 1997-195225	19970603
	BR 9709650	A	19990810	BR 1997-9650	19970603
	JP 11511758	T2	19991012	JP 1997-500771	19970603
	EP 954318	A1	19991110	EP 1997-926878	19970603
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
PRAI	US 1996-657506		19960604		
	WO 1997-US9518		19970603		

AB Pharmaceutical compns. for nasal administration comprise (a) a safe and effective amt. of a glucocorticoid selected from the group consisting of beclomethasone, flunisolide, fluticasone, memetasone, budesonide, pharmaceutically acceptable salts thereof and mixts. thereof; (b) a safe and effective amt. of a fast acting antihistamine selected from the group consisting of acrivastine, carbinoxamine, diphenhydramine, chloropheniramine, brompheniramine, dexchloropheniramine, doxylamine, clemastine, promethazine, trimeprazine, methdilazine, hydroxyzine, pyrilamine, rocastine, tripelennamine, meclizine, triprolidine, azatadine, cyproheptadine, phenindamine, pharmaceutically acceptable salts thereof and mixts. thereof; and (c) an aq., intranasal carrier wherein the compn. is free of capsaicin and, preferably, free of powders or granules. The present invention also relates to a method for the treatment of symptoms assocd. with seasonal or perennial allergic rhinitis comprising the administration of a safe and effective amt. of the intranasal pharmaceutical compns. of the present invention. A nasal spray contained beclomethasone dipropionate monohydrate 0.042, chlorpheniramine 0.500, Avicel RC-591 1.200, dextrose 5.100, Polysorbate 80 0.050, benzalkonium chloride 0.020, phenylethyl alc. 0.025, and water q.s. 100%.

ST nasal pharmaceutical spray steroid antihistamine; beclomethasone chlorpheniramine nasal pharmaceutical spray

IT **Nose**
(allergic rhinitis, perennial; nasal spray contg. intranasal steroid and antihistamine)

IT Adrenoceptor agonists
Antihistamines
Glucocorticoids
Steroids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nasal spray contg. intranasal steroid and antihistamine)

IT Drug delivery systems
Drug delivery systems
(nasal sprays; nasal spray contg. intranasal steroid and antihistamine)

IT Analgesics
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(non-opiate; nasal spray contg. intranasal steroid and antihistamine)

IT Anti-inflammatory agents
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nonsteroidal; nasal spray contg. intranasal steroid and antihistamine)

IT 9029-60-1, Lipoxygenase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; nasal spray contg. intranasal steroid and antihistamine)

IT 58-73-1, Diphenhydramine 59-33-6 59-42-7, Phenylephrine 60-87-7, Promethazine 68-88-2, Hydroxyzine 76-25-5, Triamcinolone acetonide 84-22-0, Tetrahydrozoline 84-96-8, Trimeprazine 86-22-6, Brompheniramine 90-82-4, Pseudoephedrine 91-81-6, Tripelennamine 113-92-8 129-03-3, Cyproheptadine 486-12-4, Triprolidine 486-16-8, Carbinoxamine 562-10-7 569-59-5 569-65-3, Meclizine 835-31-4, Naphazoline 1082-57-1, Tramazoline 1491-59-4, Oxymetazoline 1982-37-2, Methdilazine 3385-03-3, Flunisolide 3964-81-6, Azatadine 4419-39-0, Beclomethasone 14838-15-4, Phenylpropanolamine 15686-51-8, Clemastine 25523-97-1, Dexchlorpheniramine 29216-28-2, Mequitazine 34580-13-7, Ketotifen 50679-08-8, Terfenadine 51333-22-3, Budesonide 53882-12-5, Lodoxamide 58581-89-8, Azelastine 60607-34-3, Oxatomide 64294-95-7, Setastine **68844-77-9**, **Astemizole** 77011-63-3, Beclomethasone dipropionate monohydrate 79516-68-0, Levocabastine 79712-55-3, Tazifylline 79794-75-5, Loratadine **83881-51-0**, **Cetirizine** 86181-42-2, Temelastine 87848-99-5, Acrivastine 90566-53-3, Fluticasone **90729-43-4**, **Ebastine** 91833-77-1, Rocastine 121807-05-4, Acrivastine hydrochloride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nasal spray contg. intranasal steroid and antihistamine)

L94 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2003 ACS
AN 1997:542332 HCAPLUS
DN 127:210367
TI Pharmaceutical **compositions** containing a leukotriene inhibitor and loratadine for treatment of asthma, allergy, and inflammation
IN Dahlen, Sven-Erik; Scolnick, Edward M.
PA Merck & Co., Inc., USA; Dahlen, Sven-Erik; Scolnick, Edward M.
SO PCT Int. Appl., 10 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-41
ICS A61K031-44; A61K031-47; A61K031-405
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9728797	A1	19970814	WO 1997-US1799	19970204 <--
	W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2245162	AA	19970814	CA 1997-2245162	19970204 <--
	AU 9722579	A1	19970828	AU 1997-22579	19970204 <--
	AU 732671	B2	20010426		
	CN 1210465	A	19990310	CN 1997-192149	19970204 <--
	JP 11504044	T2	19990406	JP 1997-528627	19970204 <--
	BR 9707369	A	19990720	BR 1997-7369	19970204 <--
	EP 1014972	A1	20000705	EP 1997-905757	19970204 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
	NO 9803641	A	19980807	NO 1998-3641	19980807 <--
PRAI	US 1996-11328P	P	19960208 <--		
	GB 1996-8927	A	19960429 <--		
	WO 1997-US1799	W	19970204 <--		

AB A method of treating asthma, allergy and inflammation **comprises** treatment with a leukotriene inhibitor and loratadine either

concurrently in sep. doses or **combined** in a single pharmaceutical **formulation**. A film coated tablet contained **montelukast** sodium 10.4, loratadine 10.0, microcryst. cellulose 66.6, lactose monohydrate 100.0, croscarmellose sodium 6.0, and magnesium stearate in the core and hydroxypropyl methylcellulose 2.25, hydroxypropyl cellulose 1.25, and titanium dioxide 1.50 in the film coating.

ST pharmaceutical leukotriene inhibitor loratadine asthma allergy; inflammation pharmaceutical leukotriene inhibitor loratadine asthma

IT Leukotrienes
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors; pharmaceutical **compns**. contg. leukotriene inhibitor and loratadine for treatment of asthma, allergy, and inflammation)

IT Drug delivery systems
(oral; pharmaceutical **compns**. contg. leukotriene inhibitor and loratadine for treatment of asthma, allergy, and inflammation)

IT Allergy inhibitors
Anti-inflammatory agents
Antiasthmatics
(pharmaceutical **compns**. contg. leukotriene inhibitor and loratadine for treatment of asthma, allergy, and inflammation)

IT 79794-75-5, Loratadine 103177-37-3, Pranlukast 107753-78-6, Zafirlukast **151767-02-1, Montelukast** sodium 152922-64-0 159082-78-7
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical **compns**. contg. leukotriene inhibitor and loratadine for treatment of asthma, allergy, and inflammation)

L94 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2003 ACS
AN 1997:496788 HCAPLUS
DN 127:113353
TI A nasal spray containing a steroid and a antihistamine
IN Cramer, Ronald Dean
PA The Procter and Gamble Company, USA
SO Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM A61K031-57
ICS A61K031-58; A61K031-56; A61K031-495; A61K031-445; A61K031-55
ICI A61K031-56, A61K031-495; A61K031-56, A61K031-445; A61K031-56, A61K031-55; A61K031-57, A61K031-495; A61K031-57, A61K031-445; A61K031-57, A61K031-55; A61K031-58, A61K031-495
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 780127	A1	19970625	EP 1996-308852	19961205 <--

R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE
PRAI US 1995-574791 19951219 <--

AB Novel nasal spray **compns**. **comprising** a safe and effective amt. of a glucocorticosteroid and and antihistamine possessing leukotriene inhibiting properties are claimed. A nasal spray contained beclomethasone dipropionate.H2O 0.042, loratadine 0.200, Avicel RC-591 1.200, dextrose 5.100, Polysorbate-80 0.025, benzalkonium chloride 0.040, phenylethyl alc. 0.250, and distd. water q.s. 100%.

ST nasal spray steroid antihistamine; beclomethasone loratadine nasal spray

IT Allergy inhibitors

Antihistamines
Expectorants
(nasal spray contg. steroid and antihistamine)
IT Glucocorticoids
Leukotriene antagonists
Steroids, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nasal spray contg. steroid and antihistamine)
IT Drug delivery systems
Drug delivery systems
(nasal sprays; nasal spray contg. steroid and antihistamine)
IT Analgesics
(non-opiate; nasal spray contg. steroid and antihistamine)
IT Anti-inflammatory agents
(nonsteroidal; nasal spray contg. steroid and antihistamine)
IT 9029-60-1, Lipoxygenase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; nasal spray contg. steroid and antihistamine)
IT 59-42-7, Phenylephrine 76-25-5, Triamcinolone acetonide 84-22-0, Tetrahydrozoline 90-82-4, Pseudoephedrine 101-40-6, Propylhexedrine 124-94-7, Triamcinolone 526-36-3, Xylometazoline 835-31-4, Naphazoline 1082-57-1, Tramazoline 1491-59-4, Oxymetazoline 3385-03-3, Flunisolide 4419-39-0, Beclomethasone 7632-10-2 14838-15-4, Phenylpropanolamine 51333-22-3, Budesonide 58581-89-8, Azelastine 77011-63-3, Beclomethasone dipropionate monohydrate 79307-93-0, Azelastine hydrochloride 79794-75-5, Loratadine **83881-51-0**, **Cetirizine** 90566-53-3, Fluticasone 105102-22-5, Mometasone 177843-18-4
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nasal spray contg. steroid and antihistamine)

L94 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2003 ACS
AN 1995:464437 HCAPLUS
Correction of: 1993:670812
DN 122:213760
Correction of: 119:270812
TI Preparation of benzamidines and analogs as LTB4 antagonists
IN Anderskewitz, Ralf; Schromm, Kurt; Renth, Ernst Otto; Himmelsbach, Frank; Birke, Franz; Fuegner, Arnim
PA Boehringer Ingelheim KG, Germany
SO Ger. Offen., 24 pp.
CODEN: GWXXBX
DT Patent
LA German
IC ICM C07C257-18
ICS C07C311-29; C07C323-20; C07C317-22; A61K031-155; C07D311-74; C07D307-79; C07D213-81; C07D267-06; C07D267-22; A61K031-335; A61K031-44
ICI C07D405-12, C07D213-81, C07D315-00, C07D325-00; C07D409-12, C07D333-38, C07D315-00, C07D325-00
CC 25-19 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DE 4203201	A1	19930812	DE 1992-4203201	19920205 <--
WO 9316036	A1	19930819	WO 1993-EP70	19930114

W: AU, CA, CZ, FI, HU, JP, KR, NO, NZ, PL, RU, SK, UA, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

	AU 9333497	A1	19930903	AU 1993-33497	19930114
	AU 673343	B2	19961107		
	EP 625138	A1	19941123	EP 1993-902195	19930114
	EP 625138	B1	19990602		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 07503718	T2	19950420	JP 1993-513701	19930114
	HU 68419	A2	19950628	HU 1994-2291	19930114
	HU 216191	B	19990528		
	PL 173789	B1	19980430	PL 1993-304713	19930114
	PL 173781	B1	19980430	PL 1993-316750	19930114
	RU 2124002	C1	19981227	RU 1994-41836	19930114
	EP 902013	A1	19990317	EP 1998-121305	19930114
	EP 902013	B1	20011212		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
	AT 180770	E	19990615	AT 1993-902195	19930114
	ES 2132216	T3	19990816	ES 1993-902195	19930114
	SK 281016	B6	20001009	SK 1994-914	19930114
	CZ 287209	B6	20001011	CZ 1994-1886	19930114
	AT 210634	E	20011215	AT 1998-121305	19930114
	ES 2165122	T3	20020301	ES 1998-121305	19930114
	JP 2002322143	A2	20021108	JP 2002-73593	19930114
	ZA 9300733	A	19930806	ZA 1993-733	19930203
	FI 9403618	A	19940804	FI 1994-3618	19940804
	NO 9402903	A	19941003	NO 1994-2903	19940804
	US 6037377	A	20000314	US 1995-460961	19950605
	CZ 287173	B6	20001011	CZ 1997-1203	19970418
	US 6489365	B1	20021203	US 2000-484073	20000118
PRAI	DE 1992-4203201	A	19920205		
	DE 1992-4224289	A	19920723		
	DE 1992-4244241	A	19921224		
	EP 1993-902195	A3	19930114		
	JP 1993-513701	A3	19930114		
	WO 1993-EP70	A	19930114		
	US 1993-129154	B1	19931122		
	US 1994-352003	B1	19941208		
	US 1995-460961	A1	19950605		
	US 1997-779869	B1	19970106		

OS MARPAT 122:213760

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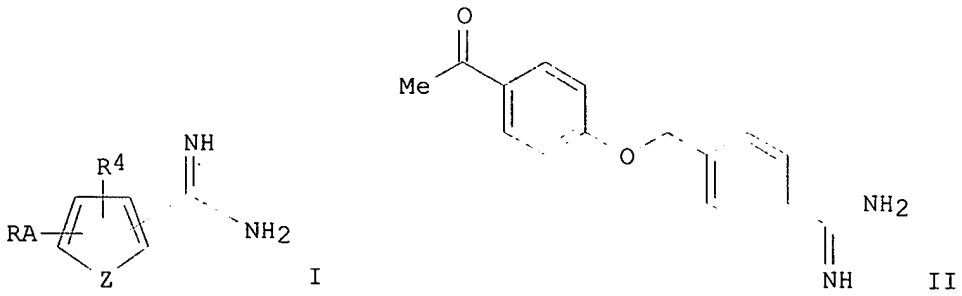

AB Title compds I [A = Z1-A1-Z2, etc.; A1 = alkylene, CH:CH, bis(methylene), etc; R = (substituted) Ph; R4 = H, halo, alkyl, aryl, etc.; Z = CH:CH, CH:N, 1,2-phenylene; Z1 = O, NH, CO, CH2, etc.; Z2 = O, NH, S] were prepd. Thus, 4-AcC6H4OH was stirred 20 h with 4-(BrCH2)C6H4CN in CHCl3 contg. EtOH and HCl and the product imido ester was treated with EtOH/NH3 to give title compd. II as the hydrochloride. II had IC50 of 0.05-0.5 .mu.M against LTB4-induced neutrophil aggregation.

ST benzamidine LTB4 antagonist prepn; antiinflammatory benzamidine prepn;

antiallergic benzamidine prepn
IT Allergy inhibitors
Bronchodilators
Inflammation inhibitors
(prepn. of benzamidines as LTB4 antagonists)
IT **Psoriasis**
(treatment; prepn. of benzamidines as LTB4 antagonists)
IT Intestine, disease
(ulcerative colitis, treatment; prepn. of benzamidines as LTB4 antagonists)
IT 151027-01-9P 151027-02-0P 151027-03-1P 151027-04-2P 151027-05-3P
151027-06-4P 151027-07-5P 151027-08-6P 151027-09-7P 151027-10-0P
151027-11-1P 151027-12-2P 151027-13-3P 151027-14-4P 151027-15-5P
151027-16-6P 151027-17-7P 151027-18-8P 151027-19-9P 151027-20-2P
151027-21-3P 151027-22-4P 151027-23-5P 151027-24-6P 151027-25-7P
151027-26-8P 151027-27-9P 151027-28-0P 151027-29-1P 151027-30-4P
151027-31-5P 151027-32-6P 151027-33-7P 151027-34-8P 151027-35-9P
151027-36-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of benzamidines as LTB4 antagonists)
IT 71160-24-2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. of benzamidines as LTB4 antagonists)
IT 99-93-4 17201-43-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of benzamidines as LTB4 antagonists)
IT 151027-37-1P 151027-38-2P 151027-39-3P 151027-40-6P 151027-41-7P
151027-42-8P 151027-43-9P 151027-44-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of benzamidines as LTB4 antagonists)

L94 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2003 ACS
AN 1994:134309 HCAPLUS
DN 120:134309
TI Quinoline derivatives as leukotriene antagonists
IN Zamboni, Robert; Guay, Daniel; Labelle, Marc
PA Merck Frosst Canada Inc., Can.
SO Eur. Pat. Appl., 14 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM C07D215-18
ICS A61K031-47
CC 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 565185	A1	19931013	EP 1993-200973	19930402 <--
	EP 565185	B1	19980708		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	US 5270324	A	19931214	US 1992-866690	19920410
	CN 1080169	A	19940105	CN 1992-105948	19920616
	CA 2092896	AA	19931011	CA 1993-2092896	19930329
	AT 168100	E	19980715	AT 1993-200973	19930402
	ES 2117691	T3	19980816	ES 1993-200973	19930402
	AU 9336863	A1	19931014	AU 1993-36863	19930408
	AU 653476	B2	19940929		
	WO 9321159	A1	19931028	WO 1993-CA156	19930408
	W: BB, BG, BR, CZ, FI, HU, KR, KZ, LK, MG, MN, MW, NO, NZ, PL, RO,				

	RU, SD, SK, UA, US				
	RW: BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	ZA 9302533	A	19931104	ZA 1993-2533	19930408
	HU 70399	A2	19951030	HU 1994-2905	19930408
	HU 218917	B	20001228		
	RU 2143426	C1	19991227	RU 1994-45911	19930408
	RO 115954	B1	20000830	RO 1994-1618	19930408
	JP 06025173	A2	19940201	JP 1993-83482	19930409
	JP 2504687	B2	19960605		
	CN 1083052	A	19940302	CN 1993-105948	19930409
	CN 1043761	B	19990623		
	ES 2080656	B1	19961016	ES 1993-1617	19930719
	ES 2080656	A1	19960201		
	FI 9404734	A	19941007	FI 1994-4734	19941007
	NO 9403792	A	19941208	NO 1994-3792	19941007
	LV 12290	B	19991120	LV 1999-68	19990426
PRAI	US 1992-866690	A	19920410		
	WO 1993-CA156	W	19930408		

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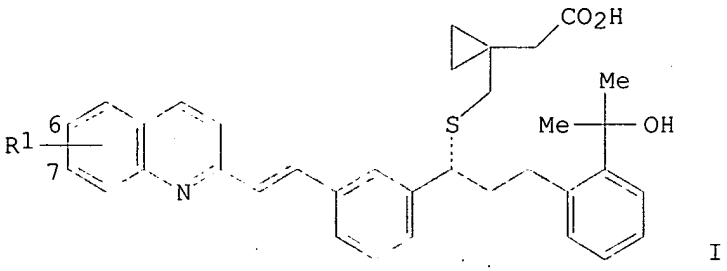

I

AB The title compds. I (R1 = 6-F or 6,7-difluoro), useful in the treatment of asthma (no data), inflammatory diseases of the eye (no data), etc., are prepd. and I-contg. formulations presented. Thus, I (R1 = 6,7-difluoro) was prepd. from 3,4-difluoroaniline in 12 steps.

ST quinoline prepn leukotriene antagonist; asthma treatment prepn quinoline; antiasthmatic prepn quinoline leukotriene antagonist

IT **Leukotrienes**
RL: RCT (Reactant); RACT (Reactant or reagent)
(**antagonists** of, quinoline derivs. as)

IT Inflammation inhibitors
(leukotriene antagonist quinoline derivs.)

IT Asthma
(treatment of, antiinflammatory quinoline deriv. leukotriene antagonists for)

IT Bronchodilators
(antiasthmatics, leukotriene antagonist quinoline derivs.)

IT Eye, disease
(uveitis, treatment of, antiinflammatory quinoline deriv. leukotriene antagonists for)

IT 152922-64-0P 152952-63-1P 152952-64-2P 152952-65-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and leukotriene antagonists activity)

IT 89729-09-9P 152922-65-1P, 6,7-Difluoro-2-methylquinoline 152922-66-2P 152922-67-3P 152922-68-4P 152922-69-5P 152922-70-8P 152922-71-9P 152922-72-0P, 1-Acetylthiomethylcyclopropaneacetonitrile 152922-73-1P 152922-74-2P 152922-86-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, in prepn. of leukotriene antagonists)

IT 1559-02-0, Diethyl-1,1-cyclopropanedicarboxylate

RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in prepn. of leukotriene antagonists derivs.)
IT 118-75-2, reactions 1128-61-6, 6-Fluoro-2-methylquinoline 3863-11-4, 3,4-Difluoroaniline 4170-30-3, 2-Butenal
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in prepn. of leukotriene-antagonists quinoline derivs.)

L94 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2003 ACS
AN 1994:77038 HCAPLUS
DN 120:77038
TI Novel amidine derivatives, their preparation, and their use as medicaments with LTB4-antagonistic effect
IN Anderskewitz, Ralf; Schromm, Kurt; Renth, Ernst Otto; Himmelsbach, Frank; Birke, Franz; Fuegner, Armin
PA Boehringer Ingelheim International G.m.b.H., Germany; Boehringer Ingelheim K.-G.
SO PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DT Patent
LA German
IC ICM C07C257-18
ICS A61K031-155; C07D311-22; C07D213-78; A61K031-35; A61K031-44
CC 25-19 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9316036	A1	19930819	WO 1993-EP70	19930114
	W: AU, CA, CZ, FI, HU, JP, KR, NO, NZ, PL, RU, SK, UA, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	DE 4203201	A1	19930812	DE 1992-4203201	19920205 <--
	DE 4224289	A1	19940127	DE 1992-4224289	19920723
	DE 4244241	A1	19940630	DE 1992-4244241	19921224
	AU 9333497	A1	19930903	AU 1993-33497	19930114
	AU 673343	B2	19961107		
	EP 625138	A1	19941123	EP 1993-902195	19930114
	EP 625138	B1	19990602		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 07503718	T2	19950420	JP 1993-513701	19930114
	PL 173789	B1	19980430	PL 1993-304713	19930114
	PL 173781	B1	19980430	PL 1993-316750	19930114
	PL 173780	B1	19980430	PL 1993-316751	19930114
	SK 281016	B6	20001009	SK 1994-914	19930114
	FI 9403618	A	19940804	FI 1994-3618	19940804
	NO 9402903	A	19941003	NO 1994-2903	19940804
	FI 2000002501	A	20001115	FI 2000-2501	20001115
PRAI	DE 1992-4203201	A	19920205		
	DE 1992-4224289	A	19920723		
	DE 1992-4244241	A	19921224		
	WO 1993-EP70	A	19930114		

OS MARPAT 120:77038
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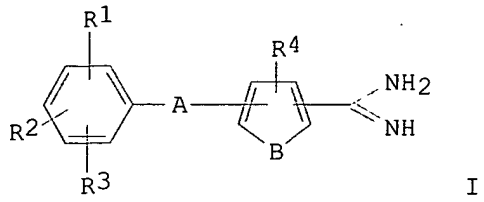
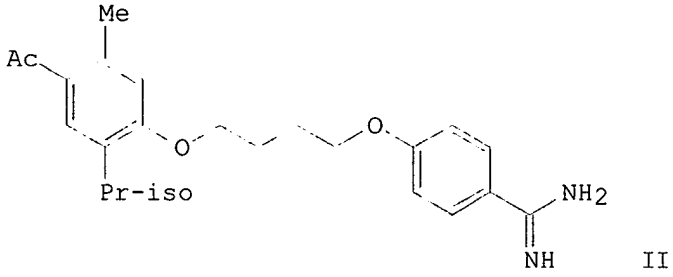


I



II

AB Amidines I [R1, R2, R3 = wide variety of groups; or adjacent R1R2 = (un)substituted CH:CHCH:CH, OCH2CH2, OCH2O, OCH2CH2O, (CH2)3-4, NHCO2, NHCOCH2O, COCH2O, COCH2CH2O; R4 = halo, (di)(alkyl)amino, OH, alkoxy; A = X1A1X2, X2A2X3, X4A2X2, OC6H4O, 1,4-piperazinediyl (Q), etc.; B = CH:CH, CH:N, S, o-C6H4; A1 = C2-4 alkylene, CH2CH:CHCH2, CH2C.tplbond.CCH2, Q1, CH2Q1CH2, (Q1 = cyclohexanediyl), etc.; A2 = C1-5 alkylene; X1 = O, NH, S, SO, SO2, CO, CH2, Q; X2 = O, NH, S, OC6H4; X3 = NHCO, CONH, SO2NH, Q; X4 = NHCO, CONH, NHSO2, SO2NH, NHCONH] and their salts were prepd. as LTB4 antagonists, for treatment of inflammatory and/or allergic conditions. For example, 4-[(4-acetyl-2-isopropyl-5-methylphenoxy)butyloxy]benzonitril e underwent Pinner reaction (i.e., HCl in EtOH to give the imidate ester hydrochloride, and subsequent ammonolysis of this with 5M NH3 in EtOH) to give amidine salt II-HCl. Several tested I inhibited binding of [3H]-LTB4 to live U937 cell receptors (Ki = 1.7-15.0 nM), inhibited LTB4-induced guinea-pig neutrophil aggregation in vitro (EC50 = 0.02-1.9 .mu.M), and inhibited LTB4-induced neutrophil accumulation in ears of mice (p.o. ED50 = 0.8-3.8 mg/kg).

ST amidine phenoxyalkoxyphenyl prepn LTB4 antagonist; leukotriene B4 antagonist amidine prepn; antiallergic amidine prepn; antiinflammatory amidine prepn

IT **Psoriasis**
(amidine LTB4 antagonists for treatment of)

IT Allergy inhibitors
Inflammation inhibitors
Ulcer inhibitors
(amidine antagonists of LTB4)

IT **Leukotrienes**
RL: RCT (Reactant); RACT (Reactant or reagent)
(**antagonists**, amidines)

IT Bronchodilators
(antiasthmatics, amidine antagonists of LTB4)

IT Amidines
RL: SPN (Synthetic preparation); PREP (Preparation)
(aryl, prepn. as antagonists of LTB4)

IT Intestine, disease
(ulcerative colitis, amidine LTB4 antagonists for treatment of)

IT 151027-40-6P 151027-42-8P 152092-86-9P 152092-87-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(Pinner reaction in prepn. of LTB4 antagonist)

IT 71160-24-2, LTB4
RL: RCT (Reactant); RACT (Reactant or reagent)

(amidine antagonists of)
IT 3524-86-5P, 4-(4-Bromobutoxy)acetophenone 49787-00-0P, 4-Hydroxybenzamidoxime 151027-43-9P, 4-Acetyl-3-methoxy-2-propylphenol 151027-44-0P, 4-(4-Bromobutylthio)benzamidine
RL: SPN (Synthetic preparation); PREP (Preparation)
(etherification in prepn. of LTB4 antagonists)
IT 151027-41-7P 152092-84-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and ammonolysis in prepn. of LTB4 antagonist)
IT 152092-85-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and hydrogenation in prepn. of LTB4 antagonist)
IT 151027-03-1 151027-04-2 151027-05-3 151027-06-4 151027-07-5
151027-08-6 151027-10-0 151027-11-1 151027-12-2 151027-13-3
151027-14-4 151027-15-5 151027-16-6 151027-17-7 151027-18-8
151027-19-9 151027-20-2 151027-21-3 151027-22-4 151027-23-5
151027-24-6 151027-25-7 151027-26-8 151027-27-9 151027-28-0
151027-29-1 151027-30-4 151027-32-6 151027-33-7 151027-34-8
151027-35-9 151027-36-0 152092-63-2 152092-64-3 152092-65-4
152092-66-5 152092-67-6 152092-68-7 152092-69-8 152092-70-1
152092-71-2 152092-72-3 152092-73-4 152092-74-5 152092-75-6
152092-76-7 152092-77-8 152092-78-9 152092-79-0 152092-80-3
152092-81-4 152092-82-5 152092-83-6 152509-27-8 152509-29-0
152510-57-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. as LTB4 antagonist)

L94 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2003 ACS
AN 1993:225676 HCAPLUS
DN 118:225676
TI Leukotriene receptor antagonist-antihistamine complex for treatment of hypersensitivity diseases
IN Ambrus, Gyorgy Ferenc; Himmelstein, Kenneth James; Woodward, David Frederick
PA Allergan, Inc., USA
SO PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-44
ICS A61K045-06
CC 1-7 (Pharmacology)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9303723	A1	19930304	WO 1992-US6559	19920806 <--
	W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
	US 5276044	A	19940104	US 1991-745232	19910814 <--
	AU 9224270	A1	19930316	AU 1992-24270	19920806 <--
	AU 658221	B2	19950406		
	EP 599943	A1	19940608	EP 1992-917850	19920806 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE				
PRAI	US 1991-745232		19910814 <--		
	WO 1992-US6559		19920806 <--		

OS MARPAT 118:225676
AB Acid-base complexes of leukotriene receptor antagonists with antihistaminics are nonirritant drugs for the treatment of hypersensitivity diseases, e.g. asthma, hay fever and allergic conjunctivitis. A complex was prepd. by reacting di-Na 2(S)-hydroxy-3(R)-[(2-carboxyethyl)thiol-3-[2-(8-

phenyloctyl)phenyl]propionate with pyrilamine-HCl in aq. soln. at pH 7.4. Pretreatment with the complex decreased the conjunctival microvascular permeability in the eye of guinea pigs treated with histamine and the leukotriene mediator LTD4.
ST hypersensitivity disease leukotriene receptor antagonist antihistaminic
IT Allergy inhibitors
(complexes of antihistaminics with leukotriene receptor antagonists as, for treatment of hypersensitivity diseases)
IT **Antihistaminics**
(complexes with leukotriene receptor antagonists, hypersensitivity diseases treatment by)
IT **Leukotrienes**
RL: BIOL (Biological study)
(**antagonists**, complexes, with antihistaminics, hypersensitivity diseases treatment by)
IT 58-73-1D, Diphenhydramine, complexes with leukotriene receptor antagonists 60-87-7D, Promethazine, complexes with leukotriene receptor antagonists 82-88-2D, complexes with leukotriene receptor antagonists 82-92-8D, Cyclizine, complexes with leukotriene receptor antagonists 82-93-9D, Chlorcyclizine, complexes with leukotriene receptor antagonists 86-21-5D, Pheniramine, complexes with leukotriene receptor antagonists 91-81-6D, Tripelennamine, complexes with leukotriene receptor antagonists 91-82-7D, Pyrrobutamine, complexes with leukotriene receptor antagonists 91-84-9D, complexes with leukotriene receptor antagonists 113-92-8D, complexes with leukotriene receptor antagonists 147-20-6D, Diphenylpyraline, complexes with leukotriene receptor antagonists 486-12-4D, Triprolidine, complexes with leukotriene receptor antagonists 522-24-7D, Fenethazine, complexes with leukotriene receptor antagonists
RL: BIOL (Biological study)
(hypersensitivity diseases treatment by)
IT 147492-90-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, for treatment of hypersensitivity diseases)

=> fil embase
FILE 'EMBASE' ENTERED AT 14:26:10 ON 09 MAR 2003

FILE COVERS 1974 TO 6 Mar 2003 (20030306/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d l109 all tot

L109 ANSWER 1 OF 5 EMBASE
AN 2000397741 EMBASE
TI Antiasthmatic effects of mediator blockade versus topical corticosteroids in allergic rhinitis and asthma.
AU Wilson A.M.; Orr L.C.; Sims E.J.; Dempsey O.J.; Lipworth B.J.
CS Prof. B.J. Lipworth, Asthma and Allergy Research Group, Ninewells Hospital/Medical School, University of Dundee, Dundee DD1 9SY, United Kingdom
SO American Journal of Respiratory and Critical Care Medicine, (2000) 162/4 I (1297-1301).
Refs: 35
ISSN: 1073-449X CODEN: AJCMED
CY United States
DT Journal; Article
FS 015 Chest Diseases, Thoracic Surgery and Tuberculosis

026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB To compare the antiasthmatic efficacy of inflammatory mediator blockade versus topical corticosteroid therapy in patients with seasonal allergic rhinitis (SAR) and asthma, 14 patients were enrolled into a single-blind, double-dummy, placebo-controlled crossover study comparing 2 wk therapy of (1) 400 .mu.g orally inhaled budesonide plus 200 .mu.g intranasal budesonide (BUD) or (2) 10 mg oral **montelukast** plus 10 mg oral **cetirizine** (ML + CZ). Before each treatment period, patients received 7 to 10 d placebo washout. All treatments were given once daily in the morning. Throughout the study, patients recorded the following domiciliary measures: peak expiratory flow (PEF), rescue inhaler requirement, asthma symptoms, and daily activity score. Laboratory measurements were made at trough of adenosine monophosphate (AMP) bronchial challenge and exhaled nitric oxide (NO). Compared with pooled placebo (PL), there were significant ($p < 0.05$) improvements in all domiciliary measures with both treatments (mean PEF [L/min] PL: 463; BUD: 478; ML + CZ: 483). For geometric mean AMP PC20 (mg/ml), there was an improvement ($p < 0.05$), compared with PL (47), for ML + CZ (133) but not for BUD (51); whereas for NO (ppb) there was significant suppression with BUD (7.6) but not ML + CZ (11.5) compared with PL (13.6). In conclusion, both combined mediator blockade and combined topical corticosteroids are equally effective antiasthma therapy in patients with asthma and SAR.
CT Medical Descriptors:
*allergic rhinitis: DT, drug therapy
*asthma: DT, drug therapy
mediator release
peak expiratory flow
inhaler
human
clinical trial
double blind procedure
single blind procedure
crossover procedure
controlled study
article
priority journal
Drug Descriptors:
*corticosteroid: CT, clinical trial
*corticosteroid: AD, drug administration
*corticosteroid: CM, drug comparison
*corticosteroid: DT, drug therapy
*corticosteroid: NA, intranasal drug administration
*corticosteroid: TP, topical drug administration
*budesonide: CT, clinical trial
*budesonide: AD, drug administration
*budesonide: CM, drug comparison
*budesonide: DO, drug dose
*budesonide: DT, drug therapy
*budesonide: IH, inhalational drug administration
*budesonide: NA, intranasal drug administration
***cetirizine: CT, clinical trial**
***cetirizine: CB, drug combination**
***cetirizine: CM, drug comparison**
***cetirizine: DT, drug therapy**
***montelukast: CT, clinical trial**
***montelukast: CB, drug combination**
***montelukast: CM, drug comparison**
***montelukast: DT, drug therapy**
adenosine phosphate

nitric oxide: EC, endogenous compound
RN (budesonide) 51333-22-3; (**cetirizine**) **83881-51-0**, 83881-52-1; (**montelukast**) 151767-02-1, **158966-92-8**; (adenosine phosphate) 61-19-8, 8063-98-7; (nitric oxide) 10102-43-9
CN (1) Pulmicort turbuhaler; (2) Rhinocort; (3) Singulair; (4) Zirtek
CO (2) Astra (United Kingdom); (3) Merck Sharp and Dohme; (4) UCB

L109 ANSWER 2 OF 5 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 2000332735 EMBASE
TI **Montelukast**, a leukotriene receptor antagonist, in combination with **loratadine**, a histamine receptor antagonist, in the treatment of chronic asthma.
AU Reicin A.; White R.; Weinstein S.F.; Finn A.F. Jr.; Nguyen H.; Peszek I.; Geissler L.; Seidenberg B.C.
CS Dr. A. Reicin, Pulmonary/Immunology, Merck Research Laboratories, RY32-649, PO Box 2000, Rahway, NJ 07065, United States
SO Archives of Internal Medicine, (11 Sep 2000) 160/16 (2481-2488). Refs: 45
ISSN: 0003-9926 CODEN: AIMDAP
CY United States
DT Journal; Article
FS 006 Internal Medicine
015 Chest Diseases, Thoracic Surgery and Tuberculosis
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English
AB Background: **Montelukast** sodium, a potent, oral, specific leukotriene-receptor antagonist, has demonstrated clinical efficacy in the treatment of chronic asthma. **Loratadine**, a selective histamine type 1 (H1)-receptor antagonist, has demonstrated antiallergic properties. Leukotriene-receptor antagonists given concomitantly with H1-receptor antagonists have been shown to have additive effects in the prevention of bronchospasm in antigen-challenge models. Objective: To determine whether **montelukast** plus **loratadine** provides improved efficacy to **montelukast** alone in the treatment of chronic asthma. Methods: The efficacy of **montelukast** alone vs **montelukast-loratadine** was studied in a 10-week, multicenter, randomized, double-blind, 2 x 2 crossover study. After a 2-week placebo run-in period, patients received **montelukast** sodium (10 mg) plus **loratadine** (20 mg), or **montelukast** sodium (10 mg) plus placebo once daily for 2 weeks. After a 2-week placebo washout period, patients were crossed over to receive 2 weeks of the other active treatment regimen, followed by another 2-week placebo washout period. Results: **Montelukast** given concomitantly with **loratadine** caused significant improvement in percentage of change from baseline in forced expiratory volume in 1 second (FEV1) compared with **montelukast** alone (13.86% vs 9.72%; P=.001). The average additional effect of **loratadine** (least square mean difference in percentage of change from baseline in FEV1) was 4.15% (95% confidence interval, 1.65%-6.65%). Key secondary end points (mean daily .beta.-agonist use, daytime and nighttime symptom scores, morning and evening peak expiratory flow rate, and the Patient Global Evaluation) all showed significant improvement with **montelukast-loratadine** (P<.05). Conclusion: **Montelukast-loratadine** significantly improved end points of asthma control during a 2-week treatment period.
CT Medical Descriptors:
*asthma: DI, diagnosis
*asthma: DT, drug therapy
drug efficacy
forced expiratory volume

drug safety
headache: SI, side effect
dyspepsia: SI, side effect
human
male
female
major clinical study
clinical trial
randomized controlled trial
double blind procedure
crossover procedure
multicenter study
controlled study
adolescent
adult
article
priority journal
Drug Descriptors:
***montelukast: AE, adverse drug reaction**
***montelukast: CT, clinical trial**
***montelukast: AD, drug administration**
***montelukast: CB, drug combination**
***montelukast: DO, drug dose**
***montelukast: DT, drug therapy**
***montelukast: PO, oral drug administration**
***loratadine: AE, adverse drug reaction**
***loratadine: CT, clinical trial**
***loratadine: CB, drug combination**
***loratadine: DO, drug dose**
***loratadine: DT, drug therapy**
antihistaminic agent: AE, adverse drug reaction
antihistaminic agent: CT, clinical trial
antihistaminic agent: CB, drug combination
antihistaminic agent: DO, drug dose
antihistaminic agent: DT, drug therapy
leukotriene receptor blocking agent: AE, adverse drug reaction
leukotriene receptor blocking agent: CT, clinical trial
leukotriene receptor blocking agent: AD, drug administration
leukotriene receptor blocking agent: CB, drug combination
leukotriene receptor blocking agent: DO, drug dose
leukotriene receptor blocking agent: DT, drug therapy
leukotriene receptor blocking agent: PO, oral drug administration
RN (**montelukast**) 151767-02-1, **158966-92-8**; (**loratadine**) 79794-75-5
CN Singulair

L109 ANSWER 3 OF 5 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 2000197224 EMBASE
TI Evaluation of treatment response in patients with seasonal allergic rhinitis using domiciliary nasal peak inspiratory flow.
AU Wilson A.; Dempsey O.J.; Sims E.J.; Coutie W.J.R.; Paterson M.C.; Lipworth B.J.
CS Prof. B.J. Lipworth, Allergy and Respiratory Medicine, Dept. of Clinic. Pharmacol./Therap., Ninewells Hosp. and Medical School, Dundee DD1 9SY, United Kingdom
SO Clinical and Experimental Allergy, (2000) 30/6 (833-838).
Refs: 18
ISSN: 0954-7894 CODEN: CLEAEN
CY United Kingdom
DT Journal; Article
FS 011 Otorhinolaryngology
026 Immunology, Serology and Transplantation
027 Biophysics, Bioengineering and Medical Instrumentation

037 Drug Literature Index
LA English
SL English
AB Background: Measurement of domiciliary nasal peak inspiratory flow rate (PIFR) may have a role in the objective assessment of treatment response in seasonal allergic rhinitis (SAR). Objective: We wished to evaluate the relationship between domiciliary measurement of nasal PIFR and a variety of symptoms associated with rhinitis. Methods Thirty-eight nonasthmatic patients, mean age (SEM) 30 years (1.4), with symptomatic SAR were evaluated in a placebo-controlled, single-blind, double-dummy, three way parallel group study. Patients received oral **cetirizine** 10 mg once daily and were randomized to receive, in addition, either: (i) intranasal mometasone furoate 200 .mu.g (n=14); (ii) oral **montelukast** 10 mg (n=11); or (iii) placebo (n=13). All treatments were given once daily for 4 weeks and were preceded by a 1 week placebo period. Domiciliary diary cards were used to record morning (am) and evening (pm) domiciliary nasal PIFR and symptom (nasal, eye, throat) scores and impact on daily activity. A total daily symptom score was then calculated from the sum of these separate symptom scores. Results: Baseline values for symptom scores and PIFR after placebo run-in were not significantly different when comparing the three groups. After 4 weeks of active treatment, there were significant ($P < 0.05$) improvements in nasal symptoms, total daily symptoms and PIFR with all treatments, with there being no significant confounding effect of pollen count, when analysed as a covariate. There were significant ($P < 0.01$) correlations for nasal symptom scores vs PIFRam ($r = - 0.51$) and PIFRpm ($r = -0.56$), and similarly for daily activity vs PIFRam ($r = -0.42$) and PIFRpm ($r = -0.48$). Conclusions: These results suggest that domiciliary measurements of nasal peak flow correlate significantly with symptoms of seasonal allergic rhinitis and may therefore be a potentially useful objective short-term marker of treatment response.
CT Medical Descriptors:
*allergic rhinitis: DI, diagnosis
*allergic rhinitis: DT, drug therapy
treatment outcome
outcomes research
device
symptomatology
scoring system
diagnostic procedure
human
male
female
clinical article
clinical trial
randomized controlled trial
single blind procedure
controlled study
adult
article
priority journal
Drug Descriptors:
***cetirizine: CT, clinical trial**
***cetirizine: CB, drug combination**
***cetirizine: CM, drug comparison**
***cetirizine: DO, drug dose**
***cetirizine: DT, drug therapy**
***cetirizine: PO, oral drug administration**
*mometasone furoate: CT, clinical trial
*mometasone furoate: CB, drug combination
*mometasone furoate: CM, drug comparison
*mometasone furoate: DO, drug dose
*mometasone furoate: DT, drug therapy

*mometasone furoate: NA, intranasal drug administration
***montelukast: CT, clinical trial**
***montelukast: CB, drug combination**
***montelukast: CM, drug comparison**
***montelukast: DO, drug dose**
***montelukast: DT, drug therapy**
***montelukast: PO, oral drug administration**
placebo
RN (**cetirizine**) **83881-51-0**, 83881-52-1; (mometasone furoate) 83919-23-7; (**montelukast**) 151767-02-1, **158966-92-8**
CN (1) Zirtek; (2) Nasonex; (3) Singulair
NP (1) In-check
CO (1) UCB (United Kingdom); (2) Schering Plough (United Kingdom); (3) Merck Sharp and Dohme (United Kingdom)
CO (1) Clement Clarke (United Kingdom)

L109 ANSWER 4 OF 5 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 2000187564 EMBASE
TI Concomitant **montelukast** and **loratadine** as treatment for seasonal allergic rhinitis: A randomized, placebo-controlled clinical trial.
AU Meltzer E.O.; Malmstrom K.; Lu S.; Prenner B.M.; Wei L.X.; Weinstein S.E.; Wolfe J.D.; Reiss T.E.
CS Dr. K. Malmstrom, Merck Research Laboratories, PO Box 2000, Rahway, NJ 07065, United States
SO Journal of Allergy and Clinical Immunology, (2000) 105/5 (917-922).
Refs: 23
ISSN: 0091-6749 CODEN: JACIBY
CY United States
DT Journal; Article
FS 030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB Background: Nasal challenge studies have suggested histamine and cysteinyl leukotrienes are important proinflammatory mediators in allergic rhinitis. This study was designed to determine the efficacy of **montelukast**, a cysteinyl leukotriene receptor antagonist, administered alone or concomitantly with **loratadine**, an H1-receptor antagonist, in seasonal allergic rhinitis. Objective: The purpose of this study was to determine the effect of concomitant use of **montelukast** and **loratadine** in the treatment of seasonal allergic rhinitis. Methods: In this multicenter (N = 12) double- blind, randomized, parallel-group, placebo-controlled 2-week trial, 460 men and women, aged 15 to 75 years, with spring seasonal allergic rhinitis were randomly allocated to receive 1 of the following 5 treatments: **montelukast** 10 or 20 mg, **loratadine** 10 mg, **montelukast** 10 mg with **loratadine** 10 mg, or placebo, once daily in the evening. The primary end point was daytime nasal symptoms score (average of congestion, rhinorrhea, itching, and sneezing). Other end points were eye symptoms, nighttime symptoms, individual daytime nasal symptoms, global evaluations (patient's and physician's), and rhinoconjunctivitis quality-of-life scores. Results: Concomitant **montelukast** with **loratadine** improved the primary end point significantly ($P < .001$) compared with placebo and each agent alone. Compared with placebo, **montelukast** with **loratadine** also significantly improved eye symptoms, nighttime symptoms, individual daytime nasal symptoms, global evaluations, and quality of life. **Montelukast** alone and **loratadine** alone caused modest improvements in rhinitis end points. All treatments were similarly well tolerated. Conclusions: Concomitant **montelukast** with **loratadine** provided effective treatment for seasonal allergic rhinitis and associated eye symptoms with a safety

profile comparable with placebo.
CT Medical Descriptors:
*allergic rhinitis: DT, drug therapy
drug efficacy
drug mixture
scoring system
nose congestion
rhinorrhea
sneezing
rhinoconjunctivitis
quality of life
drug tolerability
human
male
female
major clinical study
clinical trial
randomized controlled trial
double blind procedure
multicenter study
controlled study
adolescent
aged
adult
article
priority journal
Drug Descriptors:
***montelukast: CB, drug combination**
***montelukast: CM, drug comparison**
***montelukast: DO, drug dose**
***montelukast: DT, drug therapy**
***loratadine: CB, drug combination**
***loratadine: DO, drug dose**
***loratadine: DT, drug therapy**
*placebo: CM, drug comparison
RN (**montelukast**) 151767-02-1, **158966-92-8**; (**loratadine**) 79794-75-5

L109 ANSWER 5 OF 5 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 2000153791 EMBASE
TI **Montelukast**: A review of its therapeutic potential in persistent asthma.
AU Jarvis B.; Markham A.
CS B. Jarvis, Adis International Limited, 41 Centorian Drive, Mairangi Bay, Auckland 10, New Zealand. demail@adis.co.nz
SO Drugs, (2000) 59/4 (891-928).
Refs: 237
ISSN: 0012-6667 CODEN: DRUGAY
CY New Zealand
DT Journal; General Review
FS 015 Chest Diseases, Thoracic Surgery and Tuberculosis
030 Pharmacology
038 Adverse Reactions Titles
036 Health Policy, Economics and Management
037 Drug Literature Index
LA English
SL English
AB **Montelukast** is a cysteinyl leukotriene receptor antagonist used to treat persistent asthma in patients aged .gtoreq.6 years. The drug has a rapid onset of action. Improvements in lung function and reductions in as-needed .beta.2-agonist usage are apparent within 1 day of initiating **montelukast** treatment in adults and adolescents (aged .gtoreq.15 years treated with 10 mg/day) or children (aged 6 to 14 years treated with

5 mg/day) with persistent asthma as shown in clinical trials. In two 12-week, multicentre, randomised, double-blind studies in adults and adolescents aged .gtoreq.15 years with persistent asthma [forced expiratory volume in 1 second (FEV1) = 50 to 85% predicted] there was significantly (p .ltoreq. 0.05) greater improvement in FEV1, symptom scores, peak expiratory flow (PEF), as-needed .beta.2-agonist use, peripheral eosinophil counts and health-related quality of life (QOL) in patients treated with **montelukast** 10 mg/day than in recipients of placebo. Improvements were significantly greater in patients treated with inhaled beclomethasone 400 .mu.g/day than in recipients of **montelukast** 10 mg/day in 1 of these studies. Nonetheless, 42% of **montelukast** recipients experienced .gtoreq.11% improvement in FEV1, the median improvement in this parameter in beclomethasone-treated patients. In an 8-week multicentre, randomised, double-blind, study in children aged 6 to 14 years with persistent asthma (FEV1 50 to 85% predicted), **montelukast** 5 mg/day produced significantly greater improvements in FEV1, clinic PEF, as-needed .beta.2-agonist use, peripheral eosinophil counts, asthma exacerbations and QOL scores than placebo. The combination of **montelukast** 10 mg/day plus inhaled beclomethasone 200.mu.g twice daily provided significantly better asthma control than inhaled beclomethasone 200.mu.g twice daily in adults with poorly controlled asthma (mean FEV1 = 72% predicted) despite 4 weeks treatment with inhaled beclomethasone. Patients receiving the combination experienced significant improvements in FEV1 and morning PEF, significant reductions in daytime symptom scores, as-needed .beta.2 agonist usage and night-time awakenings with asthma, and had significantly lower peripheral blood eosinophil counts after 16 weeks in this multicentre, randomised, double-blind, placebo-controlled study. Among adults (FEV1.gtoreq.70%) treated with **montelukast** 10 mg/day for 12 weeks, inhaled corticosteroid dosages were titrated downward by 47% (vs 30% in placebo recipients), 40% of patients were tapered off of inhaled corticosteroids (vs 29%), and significantly fewer patients (16 vs 30%) experienced failed corticosteroid rescues in a multicentre, randomised, double-blind study. During clinical studies, the frequency of adverse events in **montelukast**-treated adults, adolescents and children was similar to that in placebo recipients. In conclusion, **montelukast** is well tolerated and effective in adults and children aged .gtoreq.6 years with persistent asthma including those with exercise-induced bronchoconstriction and/or aspirin sensitivity. Furthermore, **montelukast** has glucocorticoid sparing properties. Hence, **montelukast**, as monotherapy in patients with mild persistent asthma, or as an adjunct to inhaled corticosteroids is useful across a broad spectrum of patients with persistent asthma.

CT Medical Descriptors:
*asthma: DT, drug therapy
*asthma: PC, prevention
human
clinical trial
meta analysis
nonhuman
drug receptor binding
drug effect
eosinophil
bronchospasm
lung function
drug absorption
drug distribution
drug metabolism
drug excretion
drug tolerability
quality of life
drug inhibition
bronchodilatation

pharmacodynamics
drug potentiation
headache: SI, side effect
dose response
Churg Strauss syndrome
review
Drug Descriptors:
***montelukast: DT, drug therapy**
***montelukast: CM, drug comparison**
***montelukast: CT, clinical trial**
***montelukast: CB, drug combination**
***montelukast: PD, pharmacology**
***montelukast: IV, intravenous drug administration**
***montelukast: PO, oral drug administration**
***montelukast: PK, pharmacokinetics**
***montelukast: AE, adverse drug reaction**
***montelukast: DO, drug dose**
peptidoleukotriene: EC, endogenous compound
beclometasone: DT, drug therapy
beclometasone: IH, inhalational drug administration
beclometasone: CM, drug comparison
beclometasone: CB, drug combination
beclometasone: CT, clinical trial
beclometasone: DO, drug dose
corticosteroid: DT, drug therapy
corticosteroid: IH, inhalational drug administration
corticosteroid: CT, clinical trial
corticosteroid: CB, drug combination
corticosteroid: DO, drug dose
corticosteroid: PO, oral drug administration
nitric oxide: EC, endogenous compound
salbutamol: DT, drug therapy
salbutamol: IH, inhalational drug administration
salmeterol: DT, drug therapy
salmeterol: IH, inhalational drug administration
salmeterol: CM, drug comparison
salmeterol: CB, drug combination
salmeterol: CT, clinical trial
cytochrome P450 isoenzyme: EC, endogenous compound
warfarin: DT, drug therapy
warfarin: CB, drug combination
warfarin: PK, pharmacokinetics
digoxin: DT, drug therapy
digoxin: CB, drug combination
digoxin: PK, pharmacokinetics
terfenadine: DT, drug therapy
terfenadine: CB, drug combination
terfenadine: PK, pharmacokinetics
fexofenadine: DT, drug therapy
fexofenadine: PK, pharmacokinetics
fexofenadine: CB, drug combination
ethinylestradiol plus norethisterone: DT, drug therapy
ethinylestradiol plus norethisterone: CB, drug combination
ethinylestradiol plus norethisterone: PK, pharmacokinetics
theophylline: DT, drug therapy
theophylline: PK, pharmacokinetics
theophylline: CT, clinical trial
theophylline: IV, intravenous drug administration
theophylline: CB, drug combination
theophylline: PO, oral drug administration
prednisone: DT, drug therapy
prednisone: CB, drug combination
prednisone: PO, oral drug administration

prednisone: PK, pharmacokinetics
prednisolone: DT, drug therapy
prednisolone: CB, drug combination
prednisolone: PK, pharmacokinetics
prednisolone: IV, intravenous drug administration
phenobarbital: DT, drug therapy
phenobarbital: CB, drug combination
phenobarbital: IT, drug interaction
loratadine: DT, drug therapy
loratadine: CT, clinical trial
loratadine: CB, drug combination
loratadine: PO, oral drug administration
cromoglycate disodium: DT, drug therapy
cromoglycate disodium: CT, clinical trial
cromoglycate disodium: CM, drug comparison
cromoglycate disodium: IH, inhalational drug administration
nedocromil: DT, drug therapy
nedocromil: IH, inhalational drug administration
leukotriene receptor blocking agent: DT, drug therapy
leukotriene receptor blocking agent: PO, oral drug administration
pranlukast: DT, drug therapy
pranlukast: PK, pharmacokinetics
pranlukast: CM, drug comparison
zileuton: DT, drug therapy
zileuton: PO, oral drug administration

RN (**montelukast**) 151767-02-1, **158966-92-8**;
(beclometasone) 4419-39-0; (nitric oxide) 10102-43-9; (salbutamol)
18559-94-9; (salmeterol) 89365-50-4; (warfarin) 129-06-6, 2610-86-8,
3324-63-8, 5543-58-8, 81-81-2; (digoxin) 20830-75-5, 57285-89-9;
(terfenadine) 50679-08-8; (**fexofenadine**) 138452-21-8;
(ethinylestradiol plus norethisterone) 37270-71-6; (theophylline) 58-55-9,
5967-84-0, 8055-07-0, 8061-56-1, 99007-19-9; (prednisone) 53-03-2;
(prednisolone) 50-24-8; (phenobarbital) 50-06-6, 57-30-7, 8028-68-0; (
loratadine) 79794-75-5; (cromoglycate disodium) 15826-37-6,
16110-51-3, 93356-79-7, 93356-84-4; (nedocromil) 69049-73-6; (pranlukast)
103177-37-3; (zileuton) 111406-87-2, 132880-11-6

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FILE 'WPIX' ENTERED AT 14:33:28 ON 09 MAR 2003
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FILE LAST UPDATED: 7 MAR 2003 <20030307/UP>
MOST RECENT DERWENT UPDATE: 200316 <200316/DW>
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=> d all abeq tech abex tot

L119 ANSWER 1 OF 9 WPIX (C) 2003 THOMSON DERWENT
AN **2002-740979** [80] WPIX
DNC **C2002-209930**
TI Composition for treatment of asthma, particularly bronchial asthma, comprising a pair of compatible receptor antagonists and a leukotriene receptor antagonist.
DC B05
IN KAURA, S R
PA (KAUR-I) KAURA S R
CYC 100
PI WO 2002080916 A1 20021017 (200280)* EN 21p A61K031-44
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
US 2002198228 A1 20021226 (200304) A61K031-473
ADT WO 2002080916 A1 WO 2002-US10306 20020403; US 2002198228 A1 US 2001-825258 20010403
PRAI US 2001-825258 20010403
IC ICM A61K031-44; A61K031-473
ICS A61K031-135; A61K031-47
AB WO 200280916 A UPAB: 20021212
NOVELTY - Composition for the treatment of asthma comprises a first receptor antagonist and a second receptor antagonist, both being selected from leukotriene receptor antagonists and histamine receptor antagonists, and an adrenergic bronchodilator.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) a composition for the treatment of asthma comprising:
(a) a first receptor antagonist with a first chemical composition;
(b) a second receptor antagonist with a second chemical composition, where (a) and (b) are chemically dissimilar; and
(c) an adrenergic bronchodilator;
(2) a composition for the treatment of asthma comprising **montelukast** sodium, an antihistamine selected from **cetirizine**, **loratadine** and **fexofenadine**, and a sympathomimetic bronchodilator; and
(3) a method for treating asthma comprising:
(a) preparing a composition comprising a first receptor antagonist (4.0-20.0 mg), a second receptor antagonist (2.5-180.0 mg), the second receptor antagonist being different from the first; an adrenergic bronchodilator (4.0-8.0 mg); and
(b) administering the composition to a patient.
ACTIVITY - Antiinflammatory; Antiasthmatic; Respiratory.
25 Asthmatic patients were administered a composition of the invention. The asthma endpoints were studies both as primary and secondary endpoints. According to the primary endpoints, at forced expiratory volume 1 (FEV1) which were daytime endpoints, the patients showed marked improvement in both FEV1 and daytime asthma symptoms. According to the secondary endpoints, or nighttime peak expiratory flow rate, the patients

demonstrated marked improvement in this category and did not suffer as much with nocturnal awakenings due to asthmatic episodes compared with previous nights without treatment using the composition. The use of beta -agonist inhalers was significantly reduced in both the number of inhalations used daily and the percentage of days when the inhaler was actually used.

MECHANISM OF ACTION - Leukotriene Receptor Antagonist; Histamine Receptor Antagonist; Adrenergic Bronchodilator.

USE - The invention is for the treatment of respiratory disease, particularly bronchial asthma and related conditions (e.g. chronic obstructive pulmonary disease (COPD) or bronchitis), as well as any condition in which temporary inflammation of the bronchioles caused by bacterial and viral infections including inflammation of the bronchial tubes associated with both acute and chronic infection.

ADVANTAGE - The invention mitigates the adverse effects of asthma, particularly bronchial asthma. It provides flexibility of dosage schedule.

Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: B06-D01; B06-D02; B06-D13; B07-D05; B07-D11; B14-K01A; B14-L08; B14-L09

TECH UPTX: 20021212

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Materials: The adrenergic bronchodilator is a beta2-adrenergic bronchodilator, preferably albuterol sulfate. The leukotriene antagonist is selected from **montelukast** sodium and zafirlukast sodium. The histamine receptor (sic) is a histamine H1-receptor antagonist selected from ceterizine hydrochloride, **loratadine** and **fexofenadine**..

ABEX

ADMINISTRATION - Administration is oral. No dosage given.

L119 ANSWER 2 OF 9 WPIX (C) 2003 THOMSON DERWENT

AN **2002-500604** [53] WPIX

DNC **C2002-141828**

TI Pharmaceutical aerosol formulation comprising an alkylpolyglycoside surfactant.

DC B05 B07

IN BUCKTON, G; COLUMBANO, A; GROSVENOR, M; WIKELEY, P

PA (ASTR) ASTRAZENECA AB

CYC 100

PI WO 2002049616 A1 20020627 (200253)* EN 33p A61K009-12

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW

AU 2002016576 A 20020701 (200264) A61K009-12

ADT WO 2002049616 A1 WO 2001-SE2853 20011219; AU 2002016576 A AU 2002-16576 20011219

FDT AU 2002016576 A Based on WO 200249616

PRAI SE 2000-4750 20001219

IC ICM A61K009-12

ICS A61K047-26

AB WO 200249616 A UPAB: 20021031

NOVELTY - A pharmaceutical aerosol formulation comprises a hydrofluoroalkane propellant, a medicament for inhalation and an alkylpolyglycoside surfactant (I).

DETAILED DESCRIPTION - A pharmaceutical aerosol formulation comprises a hydrofluoroalkane propellant, a medicament for inhalation and an alkylpolyglycoside surfactant of formula (I) or its derivative.

DP = average degree of polymerisation from 1-4; and

R = 6-22C alkyl.

ACTIVITY - Respiratory.

No details of tests showing activity are given in the specification.

MECHANISM OF ACTION - None given.

USE - Administration of medicaments for inhalation, for treating respiratory and nasal disorders.

ADVANTAGE - The surfactants are highly surface active, have low ecotoxicity and improve the stability of the formulation. They can be synthesized with a range of properties such as molecular weight and degree of polymerisation.

DESCRIPTION OF DRAWING(S) - The figure shows an optical suspension characterization of beclomethasone dipropionate (BDP) + C12G2 in HFA-134a.

Dwg.1/12

FS CPI

FA AB; GI; DCN

MC CPI: B01-B02; B01-B03; B01-D01; B06-D01; B06-D02; B06-D13; B06-F01; B10-B02F; B10-B03B; B10-H02B; B12-M01A; B12-M01B; B14-K01; B14-N04

TECH UPTX: 20020820

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Medicament: The medicament is a beta2-adrenoreceptor agonist, an anticholinergic bronchdilator, or a 16,17-acetal of a pregnane derivative, especially formoterol, terbutaline, budesonide, or a formoterol/budesonide combination. Also preferred are compounds of formula Ar-CH2-CH2-NH-CR1R2-A-Z (II) and derivatives.

Ar = group of formula (i);

A = 1-12C straight or branched alkylene interrupted or terminated by one or more of S, SO, SO2, O, SO2NH, NHSO2, CR6R7, phenylmethyne, NH, CONH, NHCO, and NHCONH;

Z = 5-6 atom aryl in a single ring, optionally containing 1-3 of N, O and S, and optionally substituted to form a multiple fused ring system of up to 10 atoms, and the aryl optionally substituted by one or more of OH, halogen, 1-6C alkyl, 1-6C alkoxy, =O, NR8R9 or NO2; or Z = 3-12C cycloalkyl optionally containing 1-3 of N, O and S, optionally substituted by OH, halogen, 1-6C alkyl, 1-6C alkoxy, =O, NH2, or NO2;

R1,R2,R5-R9 = H or 1-6C alkyl;

R3,R4 = H; or

R3 + R4 = -S-, -NR8- or -CH2-.

Preferred Formulation: The formulation contains 0.001 wt.% surfactant, and 0.01-1.0 wt.% medicament.

ABEX

SPECIFIC COMPOUNDS - The use of 2 compounds as the alkylpolyglycoside is specifically claimed, e.g. n-dodecyl beta-D-maltoside(C12G2),C10d.p.2.7, or C10-12d.p.1.4 and C12-14 d.p.

The use of 5 compounds as the medicament is specifically claimed, e.g. 4-hydroxy-7-(2-(2-(3-(2-phenylethoxy)propylsulfonyl)ethylamino)ethyl)-1,3-benzothiazol-2(3H)-one, 4-hydroxy-7-(2-(2-(3-(2-phenylethoxy)propoxy)ethylamino)ethyl)-1,3-benzothiazol-2-(3H)-one, N-(2-(2-(4-hydroxy-2-oxo-3H-1,3-benzothizol-7-yl)ethylamino)ethyl)-2-(phenylethoxy)ethanesulfonamide, 4-hydroxy-7-(2-(3-(2-(2-(1-naphthalenyl)ethoxy)ethylsulfonyl)propylamino)ethyl)-1,3-benzothiazol-2(3H)-one and 3-(2-(4-hydroxy-2-oxo-3H-1,3-benzothiazol-7-yl)ethylamino)-N-(2-(2-(4-methylphenyl)ethoxy)ethyl)propanesulfonamide.

Preferred specifically claimed combinations of the medicaments include e.g. formoterol/budesonide, formoterol/fluticasone, formoterol/mometasone, salmeterol/fluticasone, formoterol/tiotropium salts, zafirlukast/formoterol, zafirlukast/budesonide, **montelukast**/formoterol, **montelukast**/budesonide, **loratadine**/**montelukast** and **loratadine**/zafirlukast, tiotropium and fluticasone, tiotropium and budesonide, tiotropium and mometasone, mometasone and salmeterol, formoterol and rofleponide, salmeterol and budesonide, salmeterol and rofleponide or tiotropium and rofleponide.

The use of 2 compounds as the propellant is specifically claimed, i.e. HFA-134a and/or HFA-227ea.

EXAMPLE - A formulation was prepared by placing beclomethasone dipropionate (BDP) (0.2 g) into a phial and adding surfactant solution (20 ml) comprising C12G2 (0.8 g/l). the suspension was incubated in a shaking bath at 25 degrees C for 3 hours. to allow adsorption of the surfactant onto the drug surface, and giving a drug-surfactant ratio of 10 mg surfactant/g drug. The suspension was centrifuged (15,000 rpm for 20 minutes) and the particles of drug-surfactant were separated from the supernatant and dried at 50 degrees C for 24 hours. The resulting formulation had concentrations of BDP + C12G2 of 0.2%, and HFA-134a to 100%. The stability of the suspension increased from 10 seconds for a control without surfactant to over one minute with it.

DEFINITIONS - Preferred Definitions:
R = 2-ethyl-1-hexylglycoside and DP = 1.6;
R = mixture of 8C and 10C alkyl chains in a ratio of 60C8:40C10, and DP = 1.5;
R = mixture of 16C and 8C chains, and DP = 1.2-1.3; or
R = mixture of 20C and 22C chains, and DP = 1.2-1.3.

L119 ANSWER 3 OF 9 WPIX (C) 2003 THOMSON DERWENT
AN **2002-479010** [51] WPIX
DNC **C2002-136224**
TI Treating and/or preventing cardiovascular disease e.g. atherosclerosis comprises **loratadine** and **montelukast**.
DC B02
IN HARRIS, A G; MEDEIROS, P T
PA (SCHE) SCHERING CORP
CYC 95
PI US 2002052388 A1 20020502 (200251)* 5p A61K031-473
WO 2002036124 A2 20020510 (200251) EN A61K031-47
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CZ DE DK DM DZ EC EE ES FI GB GD GE HR HU ID IL IN IS JP KG KR KZ LC LK LR LT LU LV MA MD MG MK MN MX MZ NO NZ PH PL PT RO RU SE SG SI SK SL TJ TM TR TT TZ UA US UZ VN YU ZA
AU 2002027240 A 20020515 (200258) A61K031-47
ADT US 2002052388 A1 Provisional US 2000-244226P 20001030, US 2001-12920 20011030; WO 2002036124 A2 WO 2001-US46596 20011026; AU 2002027240 A AU 2002-27240 20011026
FDT AU 2002027240 A Based on WO 200236124
PRAI US 2000-244226P 20001030; US 2001-12920 20011030
IC ICM A61K031-47; A61K031-473
ICS A61P009-00
AB US2002052388 A UPAB: 20020812
NOVELTY - Treating and/or preventing a cardiovascular disease comprises administering **loratadine** or its salts in combination with **montelukast** or its salts.
ACTIVITY - Cardiant; Antiarteriosclerotic; Antianginal; Cerebroprotective; Vasotropic.
MECHANISM OF ACTION - H1-histamine receptor antagonist; Leukotriene D4 antagonist.
No biological data is given.
USE - Used for treating and/or preventing cardiovascular disease, particularly atherosclerosis, ischemic heart disease or cerebrovascular disease such as coronary artery disease including angina pectoris, myocardial infarction, stroke, vascular heart disease and peripheral vascular disorders such as peripheral arterial disease and occlusive arterial disease, in patients suffering from an allergic and/or inflammatory condition e.g. seasonal allergic rhinitis, perennial allergic rhinitis, atopic dermatitis, urticaria, allergic asthma, non-allergic rhinitis, non-allergic asthma, sinusitis, colds, allergic dermatitis, chronic obstructive lung disease, and type 2 diabetes.

ADVANTAGE - The safe and effective therapy reduces serum immunoglobulin and/or eosinophil levels in patients at risk of cardiovascular disease.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B06-D02; B06-D13; B14-A02; B14-A02B3; B14-C03; B14-F01B; B14-F01D; B14-F01E; B14-F02; B14-F02D1; B14-F07; B14-G02A; B14-K01; B14-L08; B14-L10; B14-N04; B14-N16; B14-N17C; B14-S04
ABEX
ADMINISTRATION - **Loratadine** is administered in a dosage of 1-45 (particularly 10) mg/day. **Montelukast** is administered in a dosage of 5-20 (preferably 10) mg/day. Administration is oral, parenteral (including subcutaneous, intramuscular, intravenous or intraperitoneal), topical, vaginal or by inhalation (orally or intranasally) 1 or 2 times per day, preferably once a day.

EXAMPLE - None given in the source material.

L119 ANSWER 4 OF 9 WPIX (C) 2003 THOMSON DERWENT
AN 2001-523343 [58] WPIX
DNC C2001-156413
TI Composition for treating allergic and/or vasomotor rhinitis or allergic conjunctivitis by topical or oral administration, contains synergistic combination of non-sedating antihistamine and leukotriene antagonist.
DC B05
IN ENGEL, J; POPPE, H; SZELENYI, I; KUSS, H
PA (ASTA) ASTA MEDICA AG; (VIAT-N) VIATRIS GMBH & CO KG; (ENGE-I) ENGEL J; (POPP-I) POPPE H; (SZEL-I) SZELENYI I
CYC 57
PI DE 10007203 A1 20010823 (200158)* 9p A61K031-55
WO 2001060407 A2 20010823 (200158) DE A61K045-00
RW: AT BE CH CY DE DK EA ES FI FR GB GR IE IT LU MC NL PT SE TR
W: AU BG BR BY CN CZ EE GE HR HU ID IL IN IS JP KG KR KZ LT LV MK MX NO NZ PL RO RU SG SI SK TR UA UZ YU ZA
US 2001025040 A1 20010927 (200159) A61K031-55
AU 2001040584 A 20010827 (200176) A61K045-00
US 6436924 B1 20020820 (200257) A61K031-55
NO 2002003818 A 20020812 (200277) A61K000-00
SK 2002001175 A3 20021106 (200281) A61K045-00
CZ 2002002700 A3 20021113 (200282) A61K045-00
EP 1265615 A2 20021218 (200301) DE A61K031-55
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
ADT DE 10007203 A1 DE 2000-10007203 20000217; WO 2001060407 A2 WO 2001-EP1190 20010205; US 2001025040 A1 US 2001-784640 20010215; AU 2001040584 A AU 2001-40584 20010205; US 6436924 B1 US 2001-784640 20010215; NO 2002003818 A WO 2001-EP1190 20010205, NO 2002-3818 20020812; SK 2002001175 A3 WO 2001-EP1190 20010205, SK 2002-1175 20010205; CZ 2002002700 A3 WO 2001-EP1190 20010205, CZ 2002-2700 20010205; EP 1265615 A2 EP 2001-911591 20010205, WO 2001-EP1190 20010205
FDT AU 2001040584 A Based on WO 200160407; SK 2002001175 A3 Based on WO 200160407; CZ 2002002700 A3 Based on WO 200160407; EP 1265615 A2 Based on WO 200160407
PRAI DE 2000-10007203 20000217
IC ICM A61K000-00; A61K031-55; A61K045-00
ICS A61K031-47; A61P037-08
AB DE 10007203 A UPAB: 20011010
NOVELTY - Pharmaceutical composition comprises (separately or in combination):
(A) a non-sedating antihistamine (or its salt), other than compounds of the **loratadine** type;
(B) a leukotriene antagonist (or its salt) comprising (B1)

leukotriene D4 antagonists, (B2) 5-lipoxygenase inhibitors or (B3) FLAP (5-lipoxygenase activating protein) antagonists; and

(C) conventional carriers and/or extenders or auxiliaries.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(i) the use of a combination of (A)-(C) for the preparation of a medicament for use as above;

(ii) a medicament comprising (A)-(C), for use as above; and

(iii) the preparation of the medicaments, by mixing and formulating the appropriate components.

ACTIVITY - Antiallergic; antiinflammatory; ophthalmological.

In tests for inhibition of ovalbumin-induced nasal mucosal permeability in sensitized rats, the degree of inhibition was 11% using azelastine alone at 0.01 mg/kg i.p., 7% using **montelukast** alone at 0.1 mg/kg i.p. and 40% using a combination of azelastine at 0.01 mg/kg i.p. and **montelukast** at 0.1 mg/kg i.p.

MECHANISM OF ACTION - Antihistamine; leukotriene D4 antagonist; 5-lipoxygenase inhibitor; FLAP (5-lipoxygenase activating protein) antagonist.

USE - Used for treating allergic and/or vasomotor rhinitis or allergic conjunctivitis.

ADVANTAGE - The combination of (A) and (B) is synergistic, highly effective, safe and free of side-effects. (A) rapidly alleviates acute symptoms of rhinitis or conjunctivitis (e.g. redness, itching and swelling) and (B) effectively combats the inflammation which is the underlying cause of the disease.

Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: B06-H; B07-D05; B07-D11; B14-C03; B14-G02A; B14-N03; B14-N04; **B14-S09**

ABEX

SPECIFIC COMPOUNDS - (A) is azelastine (most preferred), levocabastine, **cetirizine**, **fexofenadine**, mizolastine or **astemizole**; (B1) is **montelukast**, zefirlukast or pranlukast; (B2) is zileuton, piriprost or AWD 23-115; and (B3) is MK-591, MK-886 or Bay x 1005 (all claimed).

ADMINISTRATION - The compositions contain 0.001-5% (A) and 0.01-5% of (B1), (B2) or (B3); and are formulated for topical administration (especially as a spray, nose drops or eye drops) or oral administration (all claimed). For topical administration, unit doses are 50-500 (preferably 200-400) mug of (A) and 100-2000 (preferably 200-1000) mug of (B1) or 50-2000 (preferably 200-1000) mug of (B2) or (B3), applied once or twice daily. For oral administration, daily doses are 0.5-16 (preferably 2-8) mg of (A) and 1-50 (preferably 5-10) mg of (B1), 1-6 (preferably 0.6-2) g of (B2) or 50-2000 (preferably 100-50) mg of (B3)

EXAMPLE - Nose drops comprised 0.1 g azelstine hydrochloride, 0.1 g hydroxypropyl methyl cellulose, 0.05 g sodium edetate, 0.0125 g benzalkonium chloride, sodium hydroxide to give pH 6.0, 6.6666 g 70% sorbitol solution and purified water to a total of 100 ml.

L119 ANSWER 5 OF 9 WPIX (C) 2003 THOMSON DERWENT

AN **1999-633803** [54] WPIX

DNC **C1999-185089**

TI Treating asthma using **cetirizine** and leukotriene inhibitor.

DC B02 B03

IN RUBIN, P D

PA (SEPR-N) SEPRACOR INC

CYC 87

PI WO 9952553 A1 19991021 (199954)* EN 34p A61K045-06

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZA ZW

AU 9935580 A 19991101 (200013)
EP 1071461 A1 20010131 (200108) EN A61K045-06
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
US 6384038 B1 20020507 (200235) A61K031-495
JP 2002511425 W 20020416 (200242) 32p A61K031-495
US 2002099058 A1 20020725 (200254) A61K031-495

ADT WO 9952553 A1 WO 1999-US8076 19990413; AU 9935580 A AU 1999-35580 19990413; EP 1071461 A1 EP 1999-917463 19990413, WO 1999-US8076 19990413; US 6384038 B1 US 1998-59571 19980414; JP 2002511425 W WO 1999-US8076 19990413, JP 2000-543163 19990413; US 2002099058 A1 Div ex US 1998-59571 19980414, US 2002-105331 20020326

FDT AU 9935580 A Based on WO 9952553; EP 1071461 A1 Based on WO 9952553; JP 2002511425 W Based on WO 9952553; US 2002099058 A1 Div ex US 6384038

PRAI US 1998-59571 19980414; US 2002-105331 20020326

IC ICM A61K031-495; A61K045-06
ICS A61K031-381; A61K031-404; A61K031-41; A61K031-4365; A61K031-47; A61K045-00; A61P011-06

ICI A61K031-495; A61K031-495; A61K031-495; A61K031-495; A61K031-495; A61K031:381; A61K031:404; A61K031:41; A61K031:4365; A61K031:47

AB WO 9952553 A UPAB: 19991221

NOVELTY - Treatment or prevention of asthma or its symptoms, dermatitis, allergic rhinitis, inflammation or a condition responsive to leukotriene inhibition, comprises administering **cetirizine** or its salts and a leukotriene inhibitor or its salts.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a composition comprising **cetirizine**, leukotriene inhibitor and carrier or excipient.

ACTIVITY - Antihistaminic; antiasthmatic; antiallergic; antiinflammatory; dermatological; ocular.

MECHANISM OF ACTION - H1 histamine receptor antagonist; leukotriene inhibitor.

USE - Useful for treating or preventing or managing asthma, asthma symptoms, inflammation, allergic rhinitis, other allergic disorders and dermatitis. The composition is also useful in combination with non-steroidal antiinflammatory agents or other non-narcotic analgesics for the treatment of cough, cold, cold-like and/or flu symptoms and the associated discomfort, headache, pain, fever and general malaise.

The composition is also useful for treating, preventing or managing, motion sickness, vertigo, diabetic retinopathy, small vessel complications due to diabetes and similar conditions.

ADVANTAGE - The composition reduces or prevents the adverse effects associated with the administration of other non-sedating antihistamines such as racemic **cetirizine** or an enantiomer of **cetirizine**. The **cetirizine** and leukotriene inhibitor have a synergistic effect.

Dwg.0/0

FS CPI
FA AB; DCN
MC CPI: B07-D11; B14-C03; B14-D05C; B14-G02A; B14-K01A; B14-L08; B14-N04; B14-N17C

TECH UPTX: 19991221

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: The leukotriene inhibitor comprises 5-lipoxygenase inhibitors, 5-lipoxygenase activating protein antagonists and/or leukotriene receptor antagonists. The composition also comprises a decongestant.

The 5-lipoxygenase inhibitor comprises zileuton, docebenone, piripost and/or ICI-D2318. The 5-lipoxygenase activating protein comprises MK-591 and/or MK-886. The leukotriene receptor antagonist comprises zafirlukast, **montelukast**, pranlukast, sodium 1-(((R)-(3-(2-(6,7-difluoro-2-

quinolinyl)ethynyl)phenyl)-3-(2-(2-hydroxy-2-propyl)phenyl)thio)methyl)cyc lopropaneacetate, 1-(((1(R)-(3-(2-(2,3-dichlorothieno(3,2-b)pyridin-5-yl)-(E)-ethenyl)phenyl)-3-(2-(1-hydroxy-1-methylethyl)phenyl)propyl)thio)methy l)cyclopropaneacetic acid and/or their salts.

ABEX

ADMINISTRATION - Administration is concurrently or sequentially. Administration is e.g. oral, intraoral, rectal, parenteral, epicutaneous, transdermal, subcutaneous, intramuscular, intranasal, sublingual, buccal, intradural, intraocular, intrarespiratory or by nasal inhalation. The dosage of **cetirizine** is 0.01-50 (preferably 1-30) mg/day, in a single or divided doses. Decongestant, e.g. pseudoephedrine, is administered at 50-300 (preferably 150-250) mg/day. The dosage of 5-lipoxygenase inhibitors is 20-2500 (preferably 20-800) mg/day. The oral dosage of leukotriene receptor antagonists is 2-100 (preferably 5-20) mg/day.

L119 ANSWER 6 OF 9 WPIX (C) 2003 THOMSON DERWENT
AN 1999-620293 [53] WPIX
DNC C1999-181054
TI Treatment or prevention of asthma or its symptoms, dermatitis, allergic rhinitis, inflammation or a condition responsive to leukotriene inhibition.
DC B02
IN RUBIN, P D
PA (SEPR-N) SEPRACOR INC
CYC 87
PI WO 9952555 A1 19991021 (199953)* EN 30p A61K045-06
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZA ZW
AU 9935581 A 19991101 (200013)
EP 1071462 A1 20010131 (200108) EN A61K045-06
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
US 6248308 B1 20010619 (200137) A61K009-12
US 6372197 B1 20020416 (200232) A61K009-12
JP 2002511427 W 20020416 (200242) 26p A61K031-454
US 2002086854 A1 20020704 (200247) A61K031-454
ADT WO 9952555 A1 WO 1999-US8078 19990413; AU 9935581 A AU 1999-35581 19990413; EP 1071462 A1 EP 1999-917464 19990413, WO 1999-US8078 19990413; US 6248308 B1 US 1998-59572 19980414; US 6372197 B1 Cont of US 1998-59572 19980414, US 2000-721668 20001127; JP 2002511427 W WO 1999-US8078 19990413, JP 2000-543165 19990413; US 2002086854 A1 Cont of US 1998-59572 19980414, Div ex US 2000-721668 20001127, US 2002-84250 20020228
FDT AU 9935581 A Based on WO 9952555; EP 1071462 A1 Based on WO 9952555; US 6372197 B1 Cont of US 6248308; JP 2002511427 W Based on WO 9952555; US 2002086854 A1 Cont of US 6248308, Div ex US 6372197
PRAI US 1998-59572 19980414; US 2000-721668 20001127; US 2002-84250 20020228
IC ICM A61K009-12; A61K031-454; A61K045-06
ICS A61K009-00; A61K031-415; A61P011-06; A61P017-00; A61P027-16; A61P029-00; A61P037-08
AB WO 9952555 A UPAB: 19991215
NOVELTY - Treatment or prevention of asthma or its symptoms, dermatitis, allergic rhinitis, inflammation or a condition responsive to leukotriene inhibition, comprises administering **norastemizole** or its salt and a leukkotriene inhibitor or its salt.

DETAILED DESCRIPTION - Treatment or prevention of asthma or its symptoms, dermatitis, allergic rhinitis, inflammation or a condition responsive to leukotriene inhibition comprises administering **norastemizole** or its salt and a leukotriene inhibitor or its salt

where the leukotriene inhibitor is selected from 5-lipoxygenase inhibitors, 5-lipoxygenase activating protein antagonists and/or leukotriene receptor antagonists. The composition may further comprise a decongestant.

ACTIVITY - Anti-histaminic; anti-asthmatic; anti-allergic; dermatological; anti-inflammatory.

USE - The compositions have potent anti-histaminic activity and are useful for treating, preventing or managing asthma, asthma symptoms, inflammation, allergic rhinitis and other allergic disorders, as well as dermatitis. The compositions may also be useful for treating, preventing or managing motion sickness, vertigo, diabetic retinopathy, small vessel complications due to diabetes and similar conditions. The compositions are also useful in combination with non-steroidal anti-inflammatory agents or other non-narcotic analgesics for the treatment of cough, cold, cold-like and/or flu symptoms and the discomfort, headache, pain, fever and general malaise associated with these.

ADVANTAGE - The composition may be used to treat, prevent or manage the disorders described while reducing or avoiding the adverse effects associated with the administration of other non-sedating antihistamines such as atemizole. The **norastemizole** and the leukotriene inhibitor have a synergistic effect.

Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: B06-A01; B06-B01; B06-D01; B06-D02; B06-D05; B06-F03; B10-A06; B10-B03B; B14-C01; B14-C03; B14-C04; B14-D05C; B14-K01A; B14-K01B; B14-L08; B14-L09; B14-N03; B14-N04; B14-N17C; **B14-S09**

ABEX

SPECIFIC COMPOUNDS - The 5-lipoxygenase inhibitor is selected from zileuton, docebenone, piripost and/or ICI-D2318. The 5-lipoxygenase activating protein is selected from MK-591 and/or MK-886. The leukotriene receptor antagonist is selected from zafirlukast, **montelukast**, pranlukast, sodium 1-(((R)-(3-(2-(6,7-difluoro-2-quinolinyl)ethynyl)phenyl)-3-(2-(2-hydroxy-2-propyl)phenyl)thio)methyl)cyclopropaneacetate and/or 1-(((1(R)-(3-(2-(2,3-dichlorothieno(3,2-b)pyridin-5-yl)-(E)-ethenyl)phenyl)-3-(2-(1-hydroxy-1-methylethyl)phenyl)propyl)thio)methyl)cyclopropaneacetic acid and their salts.

ADMINISTRATION - Administration may be concurrently or sequentially. Administration may be by any suitable route e.g. oral, intraoral, rectal, parenteral, epicutaneous, transdermal, subcutaneous, intramuscular, intransal, sublingual, buccal, intradural, intraocular, intrarespiratory or by nasal inhalation. Oral administration is generally preferred, but in the treatment of dermatitis, topical administration is preferred. Dosage of **norastemizole** is 1-200 (preferably 10-100) mg/day, in a single or divided doses. Decongestant, e.g. pseudoephedrine, is administered at 50-300 (preferably 150-250) mg/day. Dosage for leukotreine inhibitors depends on the compound employed e.g. for 5-lipoxygenase inhibitors, the daily dosage is 20-2500 (preferably 20-800) mg; for leukotriene receptor antagonists, daily oral dosage is 2-100 (preferably 5-20) mg.

EXAMPLE - No examples given.

L119 ANSWER 7 OF 9 WPIX (C) 2003 THOMSON DERWENT

AN 1999-611163 [52] WPIX

DNC C1999-178006

TI Treatment or prevention of asthma or its symptoms, dermatitis, allergic rhinitis, inflammation or a condition responsive to leukotriene inhibition.

DC B05

IN RUBIN, P D

PA (SEPR-N) SEPRACOR INC; (RUBI-I) RUBIN P D

CYC 87
PI WO 9952554 A1 19991021 (199952)* EN 33p A61K045-06
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZA ZW
AU 9936409 A 19991101 (200013)
BR 9909641 A 20001219 (200103) A61K045-06
NO 2000005147 A 20001107 (200103) A61K000-00
EP 1071463 A1 20010131 (200108) EN A61K045-06
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
US 6194431 B1 20010227 (200114) A01N043-42
ZA 2000005553 A 20010725 (200147) 43p A61K000-00
CN 1305385 A 20010725 (200164) A61K045-06
KR 2001042655 A 20010525 (200168) A61K045-06
MX 2000009972 A1 20010401 (200171) A61K045-06
HU 2001002239 A2 20020328 (200234) A61K031-445
JP 2002511426 W 20020416 (200242) 30p A61K031-445
US 6509353 B1 20030121 (200309) A61K031-445
ADT WO 9952554 A1 WO 1999-US8077 19990413; AU 9936409 A AU 1999-36409 19990413; BR 9909641 A BR 1999-9641 19990413, WO 1999-US8077 19990413; NO 2000005147 A WO 1999-US8077 19990413, NO 2000-5147 20001013; EP 1071463 A1 EP 1999-918515 19990413, WO 1999-US8077 19990413; US 6194431 B1 US 1998-59570 19980414; ZA 2000005553 A ZA 2000-5553 20001010; CN 1305385 A CN 1999-807374 19990413; KR 2001042655 A KR 2000-711354 20001013; MX 2000009972 A1 MX 2000-9972 20001012; HU 2001002239 A2 WO 1999-US8077 19990413, HU 2001-2239 19990413; JP 2002511426 W WO 1999-US8077 19990413, JP 2000-543164 19990413; US 6509353 B1 Div ex US 1998-59570 19980414, US 2000-722395 20001128
FDT AU 9936409 A Based on WO 9952554; BR 9909641 A Based on WO 9952554; EP 1071463 A1 Based on WO 9952554; HU 2001002239 A2 Based on WO 9952554; JP 2002511426 W Based on WO 9952554; US 6509353 B1 Div ex US 6194431
PRAI US 1998-59570 19980414; US 2000-722395 20001128
IC ICM A01N043-42; A61K000-00; A61K031-445; A61K045-06
ICS A01N043-40; A61K031-17; A61K031-35; A61K031-38; A61K031-381; A61K031-404; A61K031-41; A61K031-4365; A61K031-47; A61K045-00; A61P011-00; A61P011-06; A61P017-00; A61P027-16; A61P029-00; A61P037-08
ICI A61K031-445; A61K031-445; A61K031-445; A61K031-445; A61K031:381; A61K031:404; A61K031:4365; A61K031:47
AB WO 9952554 A UPAB: 19991210
NOVELTY - Treatment or prevention of asthma or its symptoms, dermatitis, allergic rhinitis, inflammation or a condition responsive to leukotriene inhibition, comprises administering a terfenadine metabolite and a leukotriene inhibitor or their salts.

DETAILED DESCRIPTION - Treatment or prevention of asthma or its symptoms, dermatitis, allergic rhinitis, inflammation or a condition responsive to leukotriene inhibition comprises administering a terfenadine metabolite and a leukotriene inhibitor or their salts where the leukotriene inhibitor is selected from 5-lipoxygenase inhibitors, 5-lipoxygenase activating protein antagonists and/or leukotriene receptor antagonists. The composition may further comprise a decongestant.

ACTIVITY - Antihistaminic; antiasthmatic; antiallergic; dermatological; antiinflammatory.

USE - The compositions have potent anti-histaminic activity and are useful for treating, preventing or managing asthma, asthma symptoms, inflammation, allergic rhinitis and other allergic disorders, as well as dermatitis. The compositions are also useful in combination with non-steroidal anti-inflammatory agents or other non-narcotic analgesics for the treatment and prevention of cough, cold, cold-like and/or flu symptoms and the discomfort, headache, pain, fever and general malaise

associated with these. The compositions may also be useful for treating, preventing or managing motion sickness, vertigo, diabetic retinopathy, small vessel complications due to diabetes and similar conditions . The terfenadine metabolite and the leukotriene inhibitor have a synergistic effect.

ADVANTAGE - The composition may be used to treat, prevent or manage the disorders described while reducing or avoiding the adverse effects associated with the administration of other non-sedating antihistamines including terfenadine.

Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: B06-A01; B06-B01; B06-D01; B06-D02; B06-F03; B07-D05; B10-A06; B10-B03B; B14-C01; B14-C03; B14-C04; B14-D05C; B14-K01A; B14-K01B; B14-L08; B14-L09; B14-N03; B14-N04; B14-N17C; **B14-S09**

ABEX

SPECIFIC COMPOUNDS - The terfenadine metabolite is racemic **fexofenadine** or (R) or (S) **fexofenadine** or 1-(p-(2-hydroxymethyl-2-propyl)phenyl)-4-(4-(alpha-hydroxy-alpha-phenylbenzyl)-1-piperidinyl)butanol. The 5-lipoxygenase inhibitor is zileuton, docebenone, piripost and/or ICI-D2318. The 5-lipoxygenase activating protein is MK-591 and/or MK-886. The leukotriene receptor antagonist is zafirlukast, **montelukast**, pranlukast, sodium 1-(((R)-(3-(2-(6,7-difluoro-2-quinolinyl)ethynyl)phenyl)-3-(2-(2-hydroxy-2-propyl)phenyl)thio)methyl)cyclopropaneacetate and/or 1-(((1(R)-(3-(2-(2,3-dichlorothieno(3,2-b)pyridin-5-yl)-(E)-ethenyl)phenyl)-3-(2-(1-hydroxy-1-methylethyl)phenyl)propyl)thio)methyl)cyclopropaneacetic acid and their salts.

ADMINISTRATION - Administration may be concurrently or sequentially. Administration may be by any suitable route e.g. oral, intraoral, rectal, parenteral, epicutaneous, transdermal, subcutaneous, intramuscular, intransasl, sublingual, buccal, intradural, intraocular, intrarespiratory or by nasal inhalation. Oral administration is generally preferred, but in the treatment of dermatitis topical administration is preferred. Dosage of terfenadine metabolite is 0.01-500 (preferably 20-200) mg/day, in a single or divided doses. Decongestant, e.g. pseudoephedrine, is administered at 50-300 (preferably 150-250) mg/day. Dosage for leukotreine inhibitors depends on the compound employed e.g. for 5-lipoxygenase inhibitors the daily dosage is 20-2500 (preferably 20-800) mg; for leukotriene receptor antagonists, daily oral dosage is 2-100 (preferably 5-20) mg.

EXAMPLE - No examples given.

L119 ANSWER 8 OF 9 WPIX (C) 2003 THOMSON DERWENT

AN **1999-539829** [45] WPIX

DNC **C1999-157680**

TI Composition containing leukotriene antagonist and antihistamine, used for treating respiratory and skin diseases, effective against wide range of symptoms.

DC B02 B03 B05

IN DANZIG, M R; JENSEN, P K; LORBER, R R; MEDEIROS, P T

PA (SCHE) SCHERING CORP

CYC 84

PI WO 9932125 A1 19990701 (199945)* EN 22p A61K031-55

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW

W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GD GE HR HU ID IL IN IS JP KG KR KZ LC LK LR LT LU LV MD MG MK MN MX NO NZ PL PT RO RU SE SG SI SK SL TJ TM TR TT UA US UZ VN YU

ZA 9811731 A 19990831 (199945) 17p A61K000-00

AU 9919071 A 19990712 (199950) A61K031-55

EP 1041990 A1 20001011 (200052) EN A61K031-55
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV NL PT RO SE
NO 2000003288 A 20000822 (200054) A61K031-55
BR 9814417 A 20001010 (200055) A61K031-55
CZ 2000002198 A3 20001115 (200064) A61K031-55
SK 2000000897 A3 20010212 (200112) A61K031-55
CN 1283115 A 20010207 (200129) A61K031-55
KR 2001033485 A 20010425 (200164) A61K031-55
MX 2000006254 A1 20010101 (200166) A61K031-445
JP 2001526232 W 20011218 (200203) 26p A61K031-47
HU 2001001369 A2 20020328 (200234) A61K031-55

ADT WO 9932125 A1 WO 1998-US26223 19981221; ZA 9811731 A ZA 1998-11731 19981221; AU 9919071 A AU 1999-19071 19981221; EP 1041990 A1 EP 1998-963828 19981221, WO 1998-US26223 19981221; NO 2000003288 A WO 1998-US26223 19981221, NO 2000-3288 20000622; BR 9814417 A BR 1998-14417 19981221, WO 1998-US26223 19981221; CZ 2000002198 A3 WO 1998-US26223 19981221, CZ 2000-2198 19981221; SK 2000000897 A3 WO 1998-US26223 19981221, SK 2000-897 19981221; CN 1283115 A CN 1998-812638 19981221; KR 2001033485 A KR 2000-706986 20000622; MX 2000006254 A1 MX 2000-6254 20000622; JP 2001526232 W WO 1998-US26223 19981221, JP 2000-525116 19981221; HU 2001001369 A2 WO 1998-US26223 19981221, HU 2001-1369 19981221

FDT AU 9919071 A Based on WO 9932125; EP 1041990 A1 Based on WO 9932125; BR 9814417 A Based on WO 9932125; CZ 2000002198 A3 Based on WO 9932125; JP 2001526232 W Based on WO 9932125; HU 2001001369 A2 Based on WO 9932125

PRAI US 1998-78638P 19980319; US 1997-68638P 19971223

IC ICM A61K000-00; A61K031-445; A61K031-47; A61K031-55
ICS A61K031-327; A61K031-352; A61K031-404; A61K031-4184; A61K031-4365; A61K031-4468; A61K031-454; A61K031-495; A61P011-00; A61P011-02; A61P011-06; A61P017-00; A61P017-04; A61P027-16; A61P037-08; A61P043-00

AB WO 9932125 A UPAB: 19991103

NOVELTY - A pharmaceutical composition contains at least one leukotriene antagonist and at least one antihistamine.

DETAILED DESCRIPTION - A pharmaceutical composition contains effective amounts of:

(A) at least one leukotriene antagonist selected from the following compounds and their salts:

(i) **montelukast,**

(ii) 1-(((R)-(3-(2-(6,7-difluoro-2-quinolinyl)ethenyl)phenyl)-3-(2-(2-hydroxy-2-propyl)phenyl)thio) methylcyclopropane acetic acid;

(iii) 1-(((1(R)-3(3-(2-(2,3-dichlorothieno (3,2-b) pyridin-5-yl)-(E)-ethenyl)phenyl)-3-(2-(1-hydroxy-1-methylethyl)phenyl)propyl)thio)methyl)cyclopropane acetic acid;

(iv) pranlukast;

(v) zafirlukast; or

(vi) (2-((2-(4-tert. butyl-2-thiazolyl)-5-benzofuranyl)-oxymethyl)-phenyl) acetic acid; and

(B) at least one antihistamine selected from **descarboethoxyloratidine, cetirizine, fexofenadine, ebastine, astemizole, norastemizole, epinastine, efletirizine** and their salts.

ACTIVITY - Dermatological; respiratory tract; antipruritic; antiinflammatory; antiallergic; antiasthma; analgesic; antitussive.

MECHANISM OF ACTION - Leukotriene antagonist; antihistamine.

USE - For treating diseases of the skin, the respiratory tract and/or associated symptoms (claimed). Typically the composition is effective against sneezing, itching runny nose, nasal congestion, redness of the eye, tears, itching of the ears or palate, shortness of breath, inflammation of the bronchial mucosa, reduced 'Force Expiratory Volume In One Second' (FEV1), coughs, rash, itchy skin, headaches, and aches and pains associated with seasonal or perennial allergic rhinitis, common colds, otitis, sinusitis, allergy, (allergic) asthma and/or inflammation.

ADVANTAGE - Inclusion of (B) improves the overall efficacy of (A) against the wide range of symptoms associated with respiratory disorders such as allergic rhinitis, colds and sinusitis.
Dwg.0/0

FS CPI
FA AB; DCN
MC CPI: B06-H; B07-H; B14-K01; B14-K01E; B14-L09; B14-N17
TECH UPTX: 19991103
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Components: (A) is **montelukast** or pranlukast; and (B) is **cetirizine, fexofenadine, ebastine, norastemizole, efletirizine** or especially **descarboethoxyloratidine**.
The composition optionally contains a third active ingredient (C), selected from decongestants (specifically pseudoephedrine), cough suppressants (specifically dextromethorphan), expectorant/mucolytic agents (specifically guaifenesin) and analgesics.

ABEX
ADMINISTRATION - Administration is generally oral. Unit dose is 5-500 mg for (A). An especially preferred composition comprises 10 mg **montelukast** and 5 mg or 7.5 mg **descarboethoxyloratidine**.

EXAMPLE - None given.

L119 ANSWER 9 OF 9 WPIX (C) 2003 THOMSON DERWENT
AN **1997-415060** [38] WPIX
DNC **C1997-132840**
TI Composition comprising **loratadine** and leukotriene antagonist - used for treatment of asthma, allergy and inflammation.
DC B02
IN DAHLEN, S; SCOLNICK, E M
PA (MERI) MERCK & CO INC
CYC 75
PI WO 9728797 A1 19970814 (199738)* EN 11p A61K031-41
RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AU AZ BA BB BG BR BY CA CN CU CZ EE GE HU IL IS JP KG KR KZ LC LK LR LT LV MD MG MK MN MX NO NZ PL RO RU SG SI SK TJ TM TR TT UA US UZ VN YU

AU 9722579	A	19970828	(199750)		A61K031-41
NO 9803641	A	19980807	(199846)		A61K031-47
CZ 9802487	A3	19990113	(199908)		A61K031-41
JP 11504044	W	19990406	(199924)	10p	A61K031-445
SK 9801056	A3	19990507	(199926)		A61K031-41
CN 1210465	A	19990310	(199929)		A61K031-41
BR 9707369	A	19990720	(199940)		A61K031-41
HU 9901860	A2	19991228	(200010)		A61K031-41
EP 1014972	A1	20000705	(200035) EN		A61K031-41

R: AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV NL PT RO SE SI

NZ 331160	A	20000728	(200043)		A61K031-41
KR 99082367	A	19991125	(200055)		A61K031-41
MX 9806421	A1	19990201	(200055)		A61K031-41
AU 732671	B	20010426	(200128)		A61K031-41

ADT WO 9728797 A1 WO 1997-US1799 19970204; AU 9722579 A AU 1997-22579 19970204; NO 9803641 A WO 1997-US1799 19970204, NO 1998-3641 19980807; CZ 9802487 A3 WO 1997-US1799 19970204, CZ 1998-2487 19970204; JP 11504044 W JP 1997-528627 19970204, WO 1997-US1799 19970204; SK 9801056 A3 WO 1997-US1799 19970204, SK 1998-1056 19970204; CN 1210465 A CN 1997-192149 19970204; BR 9707369 A BR 1997-7369 19970204, WO 1997-US1799 19970204; HU 9901860 A2 WO 1997-US1799 19970204, HU 1999-1860 19970204; EP 1014972 A1 EP 1997-905757 19970204, WO 1997-US1799 19970204; NZ 331160 A NZ 1997-331160 19970204, WO 1997-US1799 19970204; KR 99082367 A WO 1997-US1799 19970204, KR 1998-706097 19980807; MX 9806421 A1 MX 1998-6421 19980807; AU 732671 B AU 1997-22579 19970204

FDT AU 9722579 A Based on WO 9728797; CZ 9802487 A3 Based on WO 9728797; JP 11504044 W Based on WO 9728797; BR 9707369 A Based on WO 9728797; HU 9901860 A2 Based on WO 9728797; EP 1014972 A1 Based on WO 9728797; NZ 331160 A Based on WO 9728797; KR 99082367 A Based on WO 9728797; AU 732671 B Previous Publ. AU 9722579, Based on WO 9728797
PRAI GB 1996-8927 19960429; US 1996-11328P 19960208
REP US 4282233; US 4847275; US 5030643; US 5270324; US 5472964; US 5565473
IC ICM A61K031-41; A61K031-445; A61K031-47
ICS A61K031-40; A61K031-405; A61K031-44
AB WO 9728797 A UPAB: 19970922
Novel composition comprises as active ingredients **loratadine** and a leukotriene antagonist, selected from: (a) **montelukast** sodium; (b) sodium-1-((R)-(3-(2-(6,7-difluoro-2-quinolinyl)ethenyl)phenyl)-3-(2-(2-hydroxy-2-propyl)phenyl)thio)methylcyclopropaneacetate; (c) 1-(((1(R)-(3-(2-(2,3-dichlorothieno[3,2-b]pyridin-5-yl)-(E)-ethenyl)phenyl)-3-(2-(1-hydroxy-1-methylethyl) phenyl)propyl)thio)methyl)cyclopropaneacetic acid or a sodium salt; (d) pranlukast; and (e) zafirlukast.
USE - The formulation can be used for the treatment of asthma, allergy and inflammation (claimed).
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B06-D02; B06-D13; B06-F03; B14-C03; B14-G02A; B14-K01A

=> d his

(FILE 'HOME' ENTERED AT 13:30:15 ON 09 MAR 2003)
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 13:30:28 ON 09 MAR 2003
E HARRIS A/AU
L1 122 S E3,E14
L2 55 S E56,E57,E60,E61
L3 2 S E106,E107
E MEDEIROS P/AU
L4 7 S E4-E6,E9
L5 13116 S (SCHERING? OR PLOUGH?)/PA,CS
L6 6 S L1-L4 AND L5
L7 1 S DESCARBOETHOXYLORATIDIN?
L8 1402 S DESLORATADIN? OR CETIRIZIN? OR FEXOFENADIN? OR EBASTIN? OR AS

FILE 'REGISTRY' ENTERED AT 13:36:29 ON 09 MAR 2003
L9 8 S (DESLORATADINE OR CETIRIZINE OR FEXOFENADINE OR EBASTINE OR A
E DESCARBOETHOXYLORATIDINE/CN
L10 1 S E2
L11 8 S L9,L10
SEL RN
L12 64 S E1-E8/CRN
E MONTELUKAST/CN
L13 1 S E3
E C35H36CLNO3S/MF
L14 6 S E3 AND C6/ES AND C3/ES AND NC5-C6/ES AND 5/NR
L15 1 S L14 AND MONTELUKAST
L16 5 S L14 NOT L15
L17 3 S L16 NOT (142264-89-9 OR 142522-33-6)
L18 4 S L13,L15,L17
SEL RN
L19 6 S E1-E4/CRN
L20 1 S L12 AND L19
L21 5 S L19 NOT L20
L22 63 S L12 NOT L20

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L23          31 S L22 NOT (MXS/CI OR COMPD OR WITH)

     FILE 'HCAPLUS' ENTERED AT 13:43:53 ON 09 MAR 2003
L24        1334 S L11 OR L23
L25        1583 S L7,L8,L24
L26         208 S L18 OR L21
L27         254 S MONTELUKAST OR L26
L28          39 S L25 AND L27
L29           1 S L20
L30           2 S L1-L4 AND L28
L31           1 S L1-L4 AND L29
L32           2 S L5 AND L28,L29
L33           2 S L30-L32
                E ANTIHISTAMINE/CT
L34        6849 S E4-E7,E10-E13
                E E10+ALL
L35        4406 S E1
                E E2+ALL
L36        3750 S E4+NT
L37        6849 S L34-L36
L38        7027 S L26,L37
                E LEUKOTRIENE ANTAGONIST/CT
L39         373 S E4
                E E4+ALL
L40         401 S E4
L41         928 S L39,L40,L27
L42         282 S L38 AND L41
                E CARDIOVASCULAR/CT
L43       60712 S E5+NT
                E E5+ALL
                E E20+ALL
L44      313709 S E3+NT
                E CARDIOVASCULAR/CT
L45       16442 S E12-E13
                E E12+ALL
                E CARDIOVASCULAR/CT
                E E6+ALL
L46        6760 S E2
                E HEART/CT
L47      183960 S E3+NT
                E E113+ALL
                E E2+ALL
L48       62164 S E3+NT
                E BLOOD VESSEL/CT
L49      130122 S E3+NT
L50       83264 S E61+NT
L51        1359 S E94
                E E3+ALL
L52        3173 S E5
                E E25+ALL
                E ARTERY/CT
L53       61697 S E3+NT
L54       42148 S E110+NT
                E E110+ALL
L55         646 S E40+NT
                E VEIN/CT
L56       11677 S E3+NT
L57         282 S E59
                E E10+ALL
L58         811 S E6
                E CAPILLAR/CT
                E E11+ALL
                E E3+ALL
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L59         7069 S E6,E5+NT
L60           54 S L42 AND L43-L59
                 E RESPIRATORY TRACT/CT
L61       129842 S E3+NT
                 E E3+ALL
L62        21091 S E33+NT OR E34+NT
L63          613 S E4(L)UPPER
L64           87 S L42 AND L61-L63
                 E SKIN/CT
L65        79719 S E3+NT
                 E E3+ALL
                 E E33+ALL
L66        50649 S E3+NT
L67           34 S L42 AND L65,L66
L68           21 S L60 AND L64,L67
L69           53 S L28,L68
L70           38 S L28 AND L42,L65,L66,L60,L64,L67,L68
L71          283 S L28,L42,L64,L67,L69,L70
L72          174 S L71 AND (PD<=20001030 OR PRD<=20001030 OR AD<=20001030)
L73           93 S L72 AND (COMBIN? OR COMPOSITION OR SYNERG? OR MIX? OR ADMIX?
L74           81 S L72 NOT L73
L75            2 S L74 AND L25
L76           30 S L73 AND L25
L77           49 S L28,L76
L78           31 S L77 AND (PD<=20001030 OR PRD<=20001030 OR AD<=20001030)
L79           30 S L78 AND (COMBIN? OR COMPOSITION OR SYNERG? OR MIX? OR ADMIX?
L80            1 S L78 NOT L79
L81           28 S L79 AND L24
L82           19 S L81 AND L26
                 SEL DN AN 3 7 8 17 18 19
L83            6 S E1-E18
L84            9 S L81 NOT L82
                 SEL DN AN 5 7
L85            2 S L84 AND E19-E24
L86            8 S L29,L33,L83,L85 AND L1-L8,L24-L85
L87            8 S L86 AND (LEUKOTRIEN? OR ?HISTAMIN? OR ?LORATADIN? OR CETIRIZI
L88            6 S L87 AND MONTELUKAST
L89            8 S L87,L88

     FILE 'REGISTRY' ENTERED AT 14:14:58 ON 09 MAR 2003

     FILE 'HCAPLUS' ENTERED AT 14:16:14 ON 09 MAR 2003
L90            9 S (WO9303723 OR DE4203201 OR WO9728797 OR EP0565185 OR EP078012
L91            8 S L90 NOT L89
L92            8 S L91 AND L1-L8,L24-L91
L93            3 S L92 AND L11,L12,L18,L20,L23
L94            8 S L92,L93

     FILE 'EMBASE' ENTERED AT 14:20:40 ON 09 MAR 2003
L95         4070 S L11
L96         5076 S ?LORATADIN? OR ?LORATIDIN? OR CETIRIZIN? OR FEXOFENADIN? OR E
L97         5076 S L95,L96
L98         1026 S L18
L99         1039 S MONTELUKAST
L100        1039 S L98,L99
L101         137 S L97 AND L100
L102          57 S L101 AND PY<=2000
L103          25 S L102 AND CB/CT
L104          10 S L100 (L) CB/CT AND L102
L105          17 S L97 (L) CB/CT AND L102
L106          18 S L104,L105
L107           9 S L106 AND L104 AND L105
L108           4 S L107 NOT AB/FA
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L109          5 S L107 NOT L108
L110          9 S L106 NOT L107

     FILE 'EMBASE' ENTERED AT 14:26:10 ON 09 MAR 2003

     FILE 'WPIX' ENTERED AT 14:26:29 ON 09 MAR 2003
L111        268 S L96/BIX
L112         43 S L99/BIX
L113         20 S L111 AND L112
L114          3 S L113 AND (B14-S09 OR C14-S09 OR B12-C09 OR C12-C09)/MC
L115          3 S L113 AND P861/M0,M1,M2,M3,M4,M5,M6
L116          3 S L114,L115
L117         17 S L113 NOT L116
                SEL DN AN 2 5 6 15 16 17
L118          6 S L117 AND E25-E36
L119          9 S L116,L118

     FILE 'WPIX' ENTERED AT 14:33:28 ON 09 MAR 2003
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